Influence of maternal and sociodemographic characteristics on the accumulation of organohalogen compounds in Argentinian women. The EMASAR Study.

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Abstract

The occurrence of organohalogen compounds in venous serum from post-partum mothers from two Argentinian cities, Salta and Ushuaia, has been investigated (n = 698). 4,4’-DDE was the most abundant compound in these cities, with geometric means of 33 and 67 ng/g lipid weight, respectively. City of residence, age and parity were the main determinants of the accumulation of these compounds. Hexachlorobenzene (HCB) was the second most abundant pollutant in Ushuaia, 8.7 ng/g lipid, and β-hexachlorocyclohexane (β-HCH) in Salta, 7.8 ng/g lipid. Decabromodiphenyl ether was higher in Ushuaia than Salta, 8.2 and 4.1 ng/g lipid, respectively. The predominance of β-HCH, 4,4’-DDE and 4,4’-DDT in Salta was related with higher use of pesticides for agricultural applications. The observed higher concentrations of 4,4’-DDE and 4,4’-DDT in the mothers from rural+semi-urban sites than in urban areas were consistent with this agricultural origin. In addition, the most volatile organochlorine compounds included in this study, HCB and α-HCH, were mainly found in Ushuaia. The concentrations of the studied organohalogen pollutants in Argentina were lower than those found in other similar studies which is consistent with the location of these cities in the southern hemisphere.

Age, mainly for 4,4’-DDE and polychlorobiphenyl (PCB) congeners 138, 153 and 180, and parity, mainly for HCB, β-HCH, 4,4’-DDT and PCB congener 118, were the second main determinants of the concentrations of these compounds. Gestational weight gain also influenced on the maternal levels of HCB, β-HCH, 4,4’-DDT and PCB congeners 118, 138 and 153. Higher weight accumulation during pregnancy involved dilution of these persistent pollutants.

Body mass index (BMI) was a statistically significant determinant for 4,4’-DDT, α-HCH and PCB congeners 153 and 180. The observed direct correspondence between higher BMI and 4,4’-DDT concentrations was in agreement with the above reported inputs related with agricultural applications. The reverse correspondence of BMI with α-HCH and the PCB congeners indicated higher dilution at higher weight increase.

Keywords: Organohalogen pollutants, persistent organic pollutants, postpartum women, biomonitoring, age dependence of pollutant concentrations, parity dependence of pollutant concentrations

1. Introduction

Human exposure to organohalogen pollutants is a problem of public health concern due to the ubiquitous distribution, high environmental persistence and the adverse health effects of these compounds (Simonich et al., 1995; Wigle et al., 2008). Despite most of these pollutants have been banned or restricted, they are still found in environmental samples, food and human tissues (Hites, 2004, Arellano et al., 2014, Perelló et al., 2015). The chemical stability, hydrophobic properties, and lack of efficient metabolic processes for organism excretion provide these compounds with a strong bioaccumulation potential (Johnson-Restrepo et al., 2005). These aspects are particularly relevant for newborns because persistent organic pollutants (POPs) are able to cross the placenta leading to prenatal exposure of the foetus (Vizcaíno et al., 2014a; López-Espinosa et al., 2016), and infants come to life with an initial POP burden.

Children are more vulnerable than adults to chemical, physical, and biological hazards because they are still growing and their immune system and detoxification mechanisms are not fully developed (Olsen, 2000). Early-life exposure to POPs during pregnancy may have adverse impact on child development and health. In utero exposure has been associated with effects on foetal growth and premature delivery (Longnecker et al., 2001; Govarts et al., 2012; Casas et al., 2015; López-Espinosa et al., 2015; 2016), neurocognitive deficit (Grandjean and Landrigan, 2014; Ribas-Fito et al., 2006; Morales et al., 2008; Costa et al., 2014; Palou-Serra et al., 2014), obesity (Valvi et al., 2012; 2014), lower respiratory tract infections and wheeze (Gascon et al., 2012; Morales et al., 2012) and hormonal disruption (Chevrier et al., 2008; López-Espinosa et al., 2009; 2016; Morales et al., 2013; Wilson et al., 2016; Llop et al., 2017). The study of these compounds in venous maternal serum near pregnancy provides significant clues on the newborn intake (Vizcaino et al., 2014a).

The most abundant POPs usually found in human tissues are hexachlorobenzene (HCB), the β-isomer of hexachlorocyclohexane (β-HCH), 4,4'-dichlorodiphenyltrichloroethane (4,4'-DDT) and its main metabolite 4,4'-dichlorodiphenyldichloroethylene (4,4'-DDE) and polychlorinated bifenils (PCBs). Polybromodiphenyl ethers (PBDEs) are also important since their concentrations are increasing both in human and environmental samples (Hites, 2004).

These compounds have been mostly synthesized and used in the northern hemisphere but their strong capacity for long-range atmospheric transport has led to a global planetary distribution (Simonich et al., 1995), including the southern hemisphere (Amin et al., 2011). However, the information available on the occurrence of these compounds in the southern hemisphere is rather limited (Wenning et al., 2016 and Corsolini et al., 2009), particularly for what concerns human exposure.

The present study is devoted to contribute to fill this gap by analysis of maternal serum from Argentinian cohorts, representing postpartum mothers from the cities of Salta (n=498) and Ushuaia (n=200). The characteristics of the participant populations from these two cities are described in Økland et al. (2017). The concentrations of organochlorine compounds from these cities are compared with those in other sites in Hansen et al (2017). The present study is devoted to elucidate the influence of age, parity, body mass index, gestational weight gain and place of residence on the body burden of these compounds.

Ushuaia is the only urban settlement in the southern coast of Tierra del Fuego Island. The local economy mostly depends on tourism, trade, and industrial development (Commendatore et al., 2012). Salta is located in North Argentina, agriculture and its related industries are important. The latitudes of these cities are very different, 54°S and 24°S, involving subpolar and subtropical climates, with daily average temperatures of 1-9°C and 20°C, respectively (Luchini et al., 2002). Volatile pollutants are susceptible to long-range atmospheric transport, evaporating in warm areas and condensing in cold regions (Simonich and Hites, 1995). It should be expected to find more elevated concentrations of these pollutants in Ushuaia than in Salta if the global distillation effect is a driver of their occurrence.

2. Materials and methods

2.1 Population and study design

The present work is focused in two Argentinian regions, Salta in the North and Ushuaia in the South. Maternal blood samples (n=698) were collected randomly from April 2011 to Mars 2012 between the first and third day after delivery at the Clínica San Jorge in Ushuaia and the Hospital Público Materno Infantil in Salta Non-fasting maternal blood samples were obtained at 36±12 hours following delivery (median 1, range 0-3) considering that from the analytical perspective, one of the optimum sampling periods is the early postpartum days (Hansen et al., 2010). The POPs have been analysed in these samples. The study included also maternal questionnaire data and measurements of height and weight. This postpartum weight was used to obtain gestational weight gain estimates (GWG) by substraction from the reported weight prior to pregnancy plus 5 kg for child (average 3.5 kg), blood, placenta and fluid losses. This estimate differs from the standard methods (Gilmore and Redman, 2015) but no other data was available for this calculation.

The UiT The Arctic University of Norway and Stavanger University Hospital in Norway were responsible for the EMASAR study (Estudio del Medio Ambiente y la Salud Reproductiva; Study on the environment and reproductive health). Local partnerships were the private institution Clínica San Jorge in Ushuaia that is co-responsible with the public hospital for the in-hospital deliveries in the city and partly in the province, and the Hospital Público Materno Infantil in Salta that receives all the in-hospital deliveries in the city and the region. The Department of Environmental Chemistry, Institute of Environmental Assessment and Water Research (IDAEA-CSIC) was responsible for the chemical analyses.

The study was approved by the Ethics Committee of the Medical Association in Salta (2010/7317) and the Ministries of Health in both provinces. As required by Norwegian law, the study was then submitted to the Norwegian Regional Committee for Medical and Health Research Ethics (REC North) who also approved the study (2011/706). The study was conducted in accordance with the Helsinki declaration.

2.2 Sample preparation

Serum samples (1 mL) were placed into 10 mL centrifuge tubes and recovery standards TBB and PCB-209 were added (50-60 pg/µL). POP extraction was performed by addition of *n*-hexane (2 mL) and H_2SO_4 (3 mL), vortex mixing (1500 rpm, 30 s) and centrifugation (3500 rpm, 10 min). The supernatant *n*-hexane layer was aspirated into a second centrifuge tube using a Pasteur pipette. The acid layer was re-extracted two more times with n-hexane. All the n-hexane extracts were combined. This n-hexane solution was further purified by oxidation with 2 mL of concentrated H_2SO_4. The tubes were stirred in a vortex (1500 rpm, 90 s) and centrifuged (3500 rpm, 10 min). The acid was removed with a Pasteur pipette and more H_2SO_4 (2 mL) was added, again, which was followed by mixing and centrifuging once more. The supernatant organic phase was transferred to a conical bottomed, graduated tube and reduced to near dryness under a gentle stream of nitrogen. Then, the sample was transferred to gas chromatographic vials using three 75 µL rinses of isooctane which were then reduced to dryness under a very gentle stream of nitrogen. Finally, they were dissolved with 100 µL of

PCB-14 (internal standard) in isooctane (10 pg/ µL). MiliQ water (5-6 drops) was added before centrifugation when emulsions were formed (Grimalt et al., 2010).

Subsequent PBDEs analysis, involved isooctane evaporation under a very gentle stream of nitrogen and dissolution with 20 µL of [3-^{13}C]BDE-209 (6.5 pg/µL) and 30 µL of BDE-118 (20 pg/µL) as internal standards (Vizcaíno et al., 2009).

2.3 Analytical procedure

Nineteen organochlorine compounds (OCs), pentachlorobenzene (PeCB), HCB, α-HCH, β-HCH, γ-HCH, δ-HCH, PCB congeners 28, 52, 101, 118, 138, 153, 180, 2,4'-DDD, 4,4'-DDD, 2,4'-DDE, 4,4'-DDE, 2,4'-DDT and 4,4'-DDT, were quantified by gas chromatography and electron capture detection (GC-ECD, Agilent Technologies 7890A). The instrument was equipped with a HP-5MS capillary column (60 m length, 0.25 mm internal diameter, 0.25 µm film thicknesses; JW Scientific) protected with a retention gap. 2 µL were injected in splitless mode. Injector and detector temperatures were 250°C and 320°C, respectively. The oven temperature was held at 90°C for 2 min, increased to 130°C at 15°C/min and to 290°C at 4°C/min with a final holding time of 15 min. Ultrapure helium was used as carrier gas. Nitrogen was the make-up gas. Compound quantification was performed as described elsewhere (Carrizo et al., 2009).

A GC (Agilent Technologies 7890N) coupled to a mass spectrometer (MS, Agilent Technologies 5975C) operating in negative chemical ionisation mode (GC-NICI-MS) was used for identification and quantification of the PBDE congeners (17, 28, 47, 66, 71, 85, 99, 100, 138, 153, 154, 183, 190 and 209) and for confirmation of the peak OC identification. The instrument was equipped with a low bleed fused silica capillary column (15 m length, 0.25 mm I.D., 0.10 µm film thicknesses; DB-5MS) protected with a retention gap. One µL was injected, the oven temperature was programmed from an initial temperature of 90°C which was kept for 1.5 min followed by heating to 200°C at 40°C/min, a second increase up to 275°C at 5°C/min and a third increase to 300°C at 40°C/min. This temperature was held for 10 min and then increased to 310°C at 10°C/min with a final holding time of 2 min. Ammonia was used as reagent gas. Identification and quantification were performed by injection of PBDEs standard solutions (Vizcaíno et al., 2009).

2.4 Quality control

One procedural blank was included in each sample batch. Method detection limits were calculated from the average signals of the procedural blank levels plus three times the standard deviation. They ranged between 0.0014 and 0.027 ng/mL for the OCs and 0.012-0.098 ng/mL for the brominated compounds. The limits of quantification were calculated from the averages of the procedural blanks plus five times the standard deviation.

Method validation was made by analysis of proficiency testing materials obtained from the Arctic Monitoring and Assessment Program (AMAP Ring Test, 2014). The laboratory participates regularly in the AMAP Ring Test Proficiency Program for POPs in human serum and the results usually range within 20% of the consensus values.

2.5 Data analysis

Data analysis and graphics were performed using the statistical software R (R Development Core Team, 2016). Statistics was focused on the compounds found above limit of detection in more than 30% of the samples: HCB, α-HCH, β-HCH, 4,4'-DDE, 4,4'-DDT, PCB-118, PCB-138, PCB-153, PCB-180, BDE-153, BDE-154 and BDE-209. One-half of the limits of detection and limits of quantification were assigned to non-detected and non-quantified values, respectively.

Sample serum lipid content (TL) was calculated from the cholesterol (TC) and triglyceride (Tg) concentrations (TL (g/l) = 2.27*TC + Tg + 0.623; Phillips et al., 1989).

Geometric means (GM) and 95% confidence intervals (CI) were used for descriptive analysis (Figure 2), categorizing all the variables into groups (Table 1). Statistical differences between covariates were tested for significance using the Chi-square test (Table 1).

Before inclusion in the multivariate regression models, the compound concentrations were transformed into the natural logarithms for normalization. All variables were escalated for cross-comparison. The β coefficients and the standardized β are shown in Table 3.

These multivariate models were used to assess the effects of age, body mass index (BMI), parity and estimated GWG on the organohalogen concentrations:

$$\log(POP) = \beta_1(Age) + \beta_2(BMI) + \beta_3(Parity) + \beta_4(GWG) + \beta_5(Residence) + \beta_6(City) + \in \quad .$$

Age, parity, body mass index and gestational weight gain were used as continuous variables. City was categorized as Salta and Ushuaia, and residence as urban (first) and semi-urban plus rural (second). Semi-urban and rural were grouped together due to the few cases.

The β coefficients were transformed into relative changes (%) for better representation (Figure 3). For each variable, median serum concentrations by unit change (c) were calculated as $\left(\exp\left(c*\beta\right)-1\right)*100$ and the corresponding confidence intervals were calculated as $\left(\exp\left(c*\beta \pm z_{1-\alpha/2}*SE\left(\beta\right)\right)-1\right)*100$, using β and standard errors (SE) from the multiregression analysis and *c* set as the difference between the first and third quartile (Barrera-Gómez et al., 2015)

In addition, generalized additive models (GAM) were performed to assess the linearity of the variables (Figures S1-S3 in the supporting information). The R packages gmcV, visreg and ggplot were used for modelling and graphical display.

3. Results and discussion

3.1 Socio-demographic characteristics

Two hundred of the participating women were from Ushuaia and 498 from Salta (Table 1). The mean ages of the participants were 29 and 25 years, respectively, and the overall age range was between 15 and 45 years. The postpartum BMI encompassed a large spectrum of cases, from underweight (16.4 kg/m^2) to obesity (44.1 kg/m^2). In Ushuaia 79% of women were overweight or obese and this proportion was 57% in Salta. In 41% and 44% of the women from the Ushuaia and Salta, respectively, the actual newborn was the only descendant, in 36% and 24% it was the second child. Twenty-two percent and 30% of the women from these two cities had more than two children, respectively.

Only 25% of the mothers from Ushuaia and 19% from Salta met the recommendations of the Institute of Medicine (IOM) from the US National Academies of Sciences, Engineering and Medicine for GWG. These recommendations are related with the pre-pregnancy BMI of the women: normal weight: 11.25-15.75 kg, overweight: 6.75-11.25 kg and obese: 4.95-9.00 kg (Rasmussen et al., 2009). In Ushuaia half of the participants had a high GWG, while GWG was low in half of the participants from Salta.

Almost all participants lived in urban areas, 91% in Ushuaia and 86 % in Salta. The 9% and 13% lived in semi-urban or rural zones while just 2 participants were from an industrial site.

Concerning educational level, 48% of the participants had tertiary or university studies in Ushuaia while this group was 10% in Salta.

3.2 Organohalogen compound distributions

4,4'-DDE was found above limit of detection in almost 100% of the samples. PCB congeners 138 and 153 and 4,4'-DDT were found above limit of detection in about 90-97% of the mothers. In Ushuaia, α-HCH and HCB, 87% and 81%, respectively, were the following most abundant compounds, while in Salta the following most abundant were PCB congener 118 and β -HCH (79% and 70%, respectively). Most of the compounds were found above the limit of detection in around 50-70% and the remaining pollutants were only found in less than 48% of the serum samples (Table S1). The principal source of exposure to these compounds among the general population is diet. They are found mainly in animal products, including meat, fish, dairy products and eggs (Junqué et al., 2017; Llobet et al., 2003; Martí-Cid, et al., 2007).

Only four of the 14 PBDEs were above limit of detection in 30% of the samples. The BDE congener found in most cases was 209, 93% in Ushuaia and 42% in Salta, followed by 153, 154 and 47 (20-53%) (Table S1). In the indoor environment, these compounds are associated to dust ingestion, both at home and in the workplace (Jones-Otazo et al., 2005). Children, specifically, tend to accumulate them.

The most abundant OC in both cities was 4,4'-DDE, with GM of 33 ng/g lipid and 67 ng/g lipid in Ushuaia and Salta, respectively (Table 2, Figure 1), followed by HCB (8.7 ng/g lipid) in Ushuaia and β-HCH (7.8 ng/g lipid) in Salta. β-HCH was the most dominant HCH isomer while PCB-153 was the most abundant PCB congener in the mothers of both cities, followed by PCB-138 and PCB-118.

The most abundant BDE congener was 209, 8.2 ng/g lipid and 4.1 ng/g lipid in Ushuaia and Salta, respectively, followed by 138, 153 and 154 (Table 2).

The concentrations of β-HCH, 4,4'-DDE, 4,4'-DDT and PCB congener 118 were significantly higher in Salta than in Ushuaia ($p < 0.001$; Table 3 and Figure 1). The concentrations of DDT compounds in the mothers from the former city were two times higher than those in the second (Table 2, Figure 1) which may reflect much stronger use of organochlorine pesticides in relation to past agricultural activities. Conversely, the mothers from Ushaia showed significant higher concentrations of HCB ($p < 0.001$), α-HCH ($p < 0.001$), BDE congeners 153 ($p < 0.05$), 154

($p < 0.01$) and 209 ($p < 0.001$). The concentrations of α-HCH and BDE congener 209 in the former were two times or higher than those in the latter (Table 2, Figure 2). The most volatile compounds in this study, HCB and α-HCH, were mainly found in Ushuaia (Figure 1).

City of stay was the only determinant which significant influenced on the concentrations of the BDE congeners which were higher in Ushuaia than in Salta (Table 3). This difference suggested a higher use of furniture, computers and other recently-made material treated with PBDE as flame retardant in the former than in the latter city. The difference was also consistent with the higher proportion of participants with tertiary or university studies in Ushuaia than Salta (Table 1).

Other compounds such as most PCB congeners did not show significant differences between the two cities (Table 3, Figure 1).

Compared to other similar studies, these Argentinean postpartum women have low levels of the analysed compounds. The concentrations of 4,4'-DDE in Ushuaia were similar to those found in Norway (Hansen et al. 2010) or Brazil (Rudge et al. 2012), slightly lower than those from Salta and much lower than the levels from Asturias (Vizcaíno et al. 2014a). Sum of the studied PCBs were found to be much lower in the present study than in all the above cited sites and Bolivia (Arrebola et al., 2016). Finally, HCB showed similar concentrations in Ushuaia and Norway (Hansen et al. 2010), both polar regions with comparable climate and dietary habits. These differences are consistent with the location of these cities in the southern hemisphere in which organochlorine compounds were much less used. A more extensive comparison between the OC concentrations in the studied cohorts of these two cities and others from other geographic areas is provided in Hansen et al. (2017).

3.3. Residence

Comparison of the maternal concentrations by residence showed significant differences in Salta (Figure 2). Higher levels were observed in the mothers living in semi-urban and rural sites than in urban areas. This difference was consistent with a high use of DDT in agriculture. Higher maternal DDE concentrations in semi-urban and rural areas than in urban sites were also observed in Ushuaia although the difference was not significant. In this case, the lack of significance was due to the high dispersion of the values in the semi-urban and rural group likely as consequence of the low number of individuals (n = 17, Table 1). In any case, the 4,4'-

DDE and 4,4’-DDT concentrations in Salta was consistent with higher agricultural activities than in Ushuaia.

The maternal PCB concentrations in Salta were significantly higher in the urban group than in the combined semi-urban and rural groups (Figure 2) which suggested higher exposure to PCB contamination in the urban environment of this city.

3.4. Age

In general, the maternal concentrations of the OCs showed a positive significant correlation with age (Table 3). Old women tended to have higher levels than younger women (Figure 2). The differences were particularly significant in Salta for the PCB congeners 138, 153 and 180 and in Ushuaia for HCB and PCB congener 180 (Figure 3). Increases of the concentrations of PCBs and organochlorine pesticides with age have been observed in general population (Porta et al., 2010; Nøst et al., 2013) and maternal cohorts, e.g. cord blood (Carrizo et al., 2006; Vizcaino et al., 2010; Hansen et al., 2010; Veyhe et al., 2015)

No age dependence (Antignac et al., 2009; Jin et al., 2009; Zota et al., 2008) or higher concentrations in the young population (Gari and Grimalt, 2013) have been observed for PBDEs. In the present case, higher concentrations are observed in the younger mothers (Figure 2 and Table 3) but the differences are not significant, probably because of the short age interval of the participating individuals.

3.5. Parity

Parity records included the cases of stillbirth after week 23. Higher values were associated with significantly lower concentrations of all OCs except α-HCH (Table 3). This trend was clearly observed in Salta and to a lower extent in Ushuaia. (Figure 2). Parity has been found to be inversely correlated with plasma POPs (Polder et al., 2009; Hansen et al., 2010; Veyhe et al., 2015), breast milk concentrations (Manaca et al., 2011) and cord blood serum (Manaca et al., 2013), since delivery provides a way of eliminating part of the burden of these pollutants.

3.6. Body mass index

Significant correlations between BMI and the concentrations of some OCs were found (Table 3). However, they had different sign. While higher BMI involved higher maternal 4,4’-DDT concentrations, they corresponded to lower concentrations of α-HCH and PCB congeners 153 and 180 (Figure 2). These differential trends have been observed in the other studies. For instance, in serum from women of the Child Health and Development Study Cohort in the San Francisco Bay Area of California, PCB and 4,4'-DDE decreased with increasing BMI but heptachlor epoxide and 2,4'-DDT and 4,4'-DDT rose at higher BMI (James et al., 2002). In serum from a representative sample of the population of Catalonia most OCs increased at higher BMI but PCB congeners 153 and 180 decreased (Porta et al., 2010). In cord blood serum from a cohort in Menorca Island significantly higher concentrations of HCB and 4,4'-DDE were observed at higher BMI but no significant correlations were observed for the other compounds (Carrizo et al., 2006). In Germany, a study of breast milk found a negative relationship between BMI and lipid-adjusted PCBs but not with pesticides (Schade et al., 1998).

These discrepant correlations may reflect the pollutant composition of the predominant food sources in the studied cohorts. Higher BMI involves higher fat body burden. When POPs are absent or in very low amounts in the food sources higher BMI may involve tissue dilution and lower serum concentrations. On the contrary, POPs will tend to bioaccumulate in body tissues and higher BMI will involve higher serum concentrations. In the present study, the compounds showing direct correlations with BMI were 4,4'-DDE and 4,4'-DDT (Figure 2) which were those related with agricultural activities. In contrast, the reverse correlations of α-HCH and PCB congeners 153 and 180 may reflect past exposures but low current food pollutant concentrations.

No significant correlations between the maternal serum PBDE concentrations and BMI were found in the studied Argentinian cohorts (Table 3). Similarly, BMI was not a significant determinant of the concentrations of these pollutants in adult population from a representative Catalan cohort (Gari and Grimalt, 2013) or postmenopausal women of Quebec (Sandanger et al., 2007). However, lower serum concentrations of BDE-153 in obese elderly Swedish fishermen's wives were found at higher BMI (Weiss et al., 2006) and higher PBDE concentrations at higher BMI in cohorts of US consumers of sport-caught fish (Anderson et al., 2008) and pregnant women from Monterrey County (California, USA, Chamacos cohort, Castorina et al., 2011) were observed.

3.7. Gestational weight gain

The distribution of total GWG estimated was grouped according to the IOM recommendations as low, recommended and high. Since the method of estimation of GWG used in this study was using post-partum weight, grouping by the IOM recommendations could have more dispersion errors than when using standard methods (Gilmore and Redman, 2017). However, the observed dependences of the concentrations of some compounds were significant and showed clear trends. Thus, the observed data could be interpreted to indicate a clear dependence between concentrations of some pollutants and GWG of the women from this cohort which would be better defined if this weight parameter had been calculated following a more standard procedure. HCB and PCB congeners 118, 138 and 153 showed substantially higher serum concentrations in the mothers whose GMG was low (Figure 2). This difference was not observed for the DDTs or PBDEs. These results were consistent with a previous study of Swedish pregnant women in which inverse relations between GWG and maternal serum concentrations of PCB congeners 118, 138, 153, 156 and 180 and HCB were found (Glynn et al., 2007) as well as for PCB congeners in mothers from Michigan and Texas (Jaacks et al., 2016) and in the Norwegian Mother and Child cohort study (Caspersen et al., 2016). This inverse relationship has also been observed when comparing GWG and cord blood (Vizcaino et al., 2014).

3.8. Multiregression analysis

Linear and non-linear multivariate models of the aforementioned variables (Table 3, Figure 3) provided an overall description of the main factors influencing on the concentrations of these organohalogen pollutants. City of residence was the main determinant, involving higher concentrations of HCB, α-HCH and PBDEs in Ushuaia and higher concentrations of β-HCH, 4,4'-DDE, 4,4'-DDT and PCB congeners 118 and 180 in Salta. This influence is consistent with a higher use of DDT and also β-HCH related with agricultural applications in the latter and a more urban life style involving higher use of PBDEs in the former. Age was the main second determinant of 4,4'-DDE and PCB congeners 138, 153 and 180 (Figure 3). Parity was the main second determinant of HCB, β-HCH, 4,4'-DDT and PCB congener 118 (Figure 3). These two determinants alternative scored as the third cause of change when the other was the second. Thus, city of residence, age and parity were clear determinants of the concentrations of these pollutants, although PBDE concentrations were only influenced by the former.

GWG was observed to be a fourth significant factor of variation which was inversely related to the maternal serum concentrations of HCB, β-HCH, 4,4'-DDT and PCB congeners 118, 138 and 153. BMI was also a determinant for PCB congeners 153 and 180, α-HCH and 4,4'-DDT.

Urban vs rural+semi-urban residence was relevant for 4,4'-DDE and 4,4'-DDT which is consistent with the above mentioned influence of agricultural uses of these compounds.

4. Conclusions

City of residence, age and parity are the main aspects determining the accumulation of OCs in the studied cohorts. The former reflects a higher use of DDT and also β-HCH related with agricultural activities in Salta and higher use of furniture and electronics treated with flame retardants in Ushuaia. Age is involving higher concentrations of the OCs when it is significantly related with the maternal accumulation of these pollutants which is consistent with difficulties of human metabolism to eliminate these compounds after intake. Parity is inversely related to the concentrations of OCs when it is a statistically significant determinant which reflects a clean detoxification of the mother into the newborns. Urban vs rural+semi-urban residence was relevant for 4,4'-DDE and 4,4'-DDT which is consistent with the above mentioned influence of agricultural uses of these compounds.

Women with low GWG had significantly higher concentrations of HCB and some PCB congeners. This determinant has a lower level of relevance for OC accumulation than those previously described. However, it is inversely related to the maternal concentrations of the OCs for all the compounds in which it is statistically significant. Higher accumulation of weight during pregnancy involves dilution of these persistent pollutants.

BMI was a statistically significant determinant for 4,4'-DDT, α-HCH and PCB congeners 153 and 180. The direct correspondence between higher BMI and the concentrations of 4,4'-DDT is in agreement with the above reported inputs of this compound related with agricultural applications. Since POPs tend to bioaccumulate in body tissues the presence of these compounds in food involves higher serum concentrations at higher BMI. The reverse correspondence of BMI with α-HCH and the PCB congeners indicate higher dilution at higher weight gain when the food incorporation of these compounds is low.

The most volatile organochlorine compounds included in the study, HCB and α-HCH, were found in higher concentration in the colder area (Ushuaia).

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References

AMAP Ring Test; www.inspq.qc.ca/en/ctq/eqas/amap/description

Amin, O. A.; Comoglio, L. I.; Sericano, J. L. Polynuclear aromatic and chlorinated hydrocarbons in mussels from the coastal zone of Ushuaia, Tierra del Fuego, Argentina. *Env. Toxicol. Chem.* **2011**, 30 (3), 521-529; DOI: 10.1002/etc.422

Anderson, H. A.; Imm, P.; Knobeloch, L.; Turyk, M.; Mathew, J.; Buelow, C.; Persky, V. Polybrominated diphenyl ethers (PBDE) in serum: findings from a US cohort of consumers of sport-caught fish. *Chemosphere* **2008**, 73, 187–194.

Antignac, J.-P.; Cariou, R.; Zalko, D.; Berrebi, A.; Cravedi, J.-P.; Maume, D.; Marchand, P.; Monteau, F.; Riu, A.; Andre, F.; Le Bizec, B. Exposure assessment of French women and their newborn to brominated flame retardants: determination of tri- to deca-polybromodiphenylethers (PBDE) in maternal adipose tissue, serum, breast milk and cord serum. *Environ. Pollut.* **2009**, 157, 164–173.

Arellano, L.; Grimalt, J. O.; Fernández, P.; López, J. F.; Nickus, U.; Thies, H. Persistent organic pollutant accumulation in seasonal snow along an altitudinal gradient in the Tyrolean Alps. *Environ. Sci. Pollut. Res.* **2014**, *21*, 12638-12650; DOI: 10.1007/s11356-014-3196-x

Arrebola, J. P.; Cuellar, M.; Bonde, J. P.; Gonzalez-Alzaga, B.; Mercado, L. A. Associations of maternal o,p'-DDT an p,p'-DDE levels with birth outcomens in a Bolivian cohort. *Environ. Res.* **2016**, 151, 469-477.

Barrera-Gómez, J.; Basagaña, X. Models with transformed variables: interpretation and software. *Epidemiol.* **2015**, 26 (2), e16-e17; DOI: 10.1097/EDE.0000000000000247.

Casas, M.; Nieuwenhuijsen, M.; Martinez, D.; Ballester, F.; Basagaña, X.; Barterrechea, M.; Chatzi, L.; Chevrier, L.; Eggesbo, M.; Fernandez, M. F.; Govarts, E.; Guxens, M.; Grimalt, J. O.;

Hertz-Picciotto, I.; Iszatt, N.; Kasper-Sonnenberg, M.; Kiviranta, H.; Kogevinas, M.; Palkovicova, L.; Ranft, U.; Schoeters, G.; Patelarou, E.; Skaalum Petersen, M.; Torrent, M.; Trnovec, T.; Valvi, D.; Vase Toft, G.; Weihe, P.; Weisglus-Kuperus, N.; Wilhelm, M.; Wittsiepe, J.; Vrijheid, M.; Bonde, J. P. Prenatal exposure to PCB-153, pp'-DDE and birth outcomes in 9000 mother-child pairs: Exposure-response relationship and effect modifiers. Environ. Internat. **2015,** 74, 23-31.

Carrizo, D.; Grimalt, J. O. Gas chromatographic-mass spectrometric analysis of polychlorostyrene congener mixtures in sediments, human sera and cord sera. *J. Chromatogr. A* **2009**, *1216*, 5723-5729; DOI: 10.1016/j.chroma.2009.05.055

Carrizo, D.; Grimalt, J. O.; Ribas-Fito, N.; Sunyer, J.; Torrent, M. Physical-chemical and maternal determinants of the accumulation of organochlorine compounds in four-year-old children. *Environ. Sci. Technol.* **2006**, *40*, 1420-1426.

Caspersen, I. H.; Kvalem, H. E.; Haugen, M.; Brantsæter, A. L.; Meltzer, H. M.; Alexander, J.; Thomsen, C.; Frøshaug, M.; Bruun Bremnes, N. M.; Broadwell, S. L.; Granum, B.; Kogevinas, M.; Knutsen, H. K. Determinants of plasma PCB, brominated flame retardants, and organochlorine pesticides in pregnant women and 3 year old children in The Norwegian Mother and Child Cohort Study. *Environ. Res.* **2016**, *146*, 136-144; DOI: 10.1016/j.envres.2015.12.020

Castorina, R.; Bradman, A.; Sjödin, A.; Fenster, L.; Jones, R. S.; Harley, K. G.; Eisen, E. A.; Eskenazi, B. Determinants of serum polybrominated diphenyl ether (PBDE) levels among pregnant women in the CHAMACOS cohort. Environ. Sci. Technol. **2011**, 45, 6553–6560.

Chevrier, J.; Eskenazi, B.; Holland, N.; Bradman, A.; Barr, D. B. Effects of exposure to polychlorinated biphenyls and organochlorine pesticides on thyroid function during pregnancy. *Am. J. Epidemiol.* **2008**, *168*, 298-310

Commendatore, M. G.; Nievas, M. L.; Amin, O.; Esteves, J. L. Sources and distribution of aliphatic and polyaromatic hydrocarbons in coastal sediments from the Ushuaia Bay (Tierra del Fuego, Patagonia, Argentina). *Mar. Environ. Res.* **2012**, 74, 20-31; DOI: 10.1016/j.marenvres.2011.11.010

Corsolini, S. Industrial contaminants in Antarctic biota. *J. Chromatogr. A* **2009**, 1216, 598-612; DOI: 10.1016/j.chroma.2008.08.012

Costa, L. G.; Laat, R.; Tagliaferri, S.; Pellacani, C. A mechanistic view of polybrominated ether (PBDE) developmental neurotoxicity. *Toxicol. Lett.* **2014**, *230*, 282-294; DOI: 10.1016/j.toxlet.2013.11.011

Garí, M.; Grimalt, J. O., Inverse age-dependent accumulation of decabromodiphenyl ether and other PBDEs in serum from a general adult population. *Environ. Int.* **2013**, 54, 119-127; DOI: 10.1016/j.envint.2013.01.012

Gascon, M.; Vrijheid, M.; Martinez, D.; Basterrechea, M.; Blarduni, E.; Esplugues, A.; Vizcaino, E.; Morales, E.; Sunyer, J. Pre-natal exposure to dichlorodiphenyldichloroethylene and infant lower respiratory tract infections and weeze. Eur. Resp. J. **2012,** 39, 1188-1196.

Gilmore L. A.; Redman, L. M. Weight Gain in Pregnancy and Application of the 2009 IOM Guidelines: Toward a Uniform Approach. *Obesity*, **2015,** *23*, 507-511.

Glynn, A.; Aune, M.; Darnerud, P. O.; Cnattingius, S.; Bjerselius, R.; Becker, W.; Lignell, S. Determinants of serum concentations of organochlorine compounds in Swedish pregnant women: a cross-sectional study. *Environ. Health*, **2007**, *6*, 2, 1-14; DOI: 10.1186/1476-069X-6-2.

Govarts, E.; Nieuwenhuijsen, M.; Schoeters, G.; Ballester, F.; Bloemen, K.; de Boer, M.; Chevrier, C.; Eggesbo, M.; Guxens, M.; Kramer, U.; Legler, J.; Martinez, D.; Palkovicova, L.; Patelarou, E.; Ranft, U.; Rautio, A.; Skaalum Petersen, M.; Slama, R.; Stigum, H.; Toft, G.; Trnovec, T.; Vandentorren, S.; Weihe, P.; Weisglas Kuperus, N.; Wilhelm, M.; Wittsiepe, J.; Bonde, J. P. Birth weight and prenatal exposure to polychlorinated biphenyls (PCBs) and dichlorodiphenyldichloroethylene (DDE): A meta-analysis within 12 European bith cohorts. Environ. Health Perspect. **2012,** 120, 162-170.

Grandjean, P.; Landrigan, P. J. Neurobehavioural effects of developmental toxicity. *Lancet Neurol.* **2014**, *13 (3)*, 330-338: DOI: 10.1016/S1474-4422(13)70278-3

Grimalt, J. O.; Howam, M.; Carrizo, D.; Otero, R.; Rodrigues de Marchi, M. R.; Vizcaíno, E. Integrated analysis of halogenated organic pollutants in sub-millilitre volumes of venous and umbilical cord blood sera. *Anal. Bioanal. Chem.* **2010**, *396*, 2265-2272; DOI: 10.1007/s00216-010-3460-y

Hansen, S.; Nieboer, E.; Odland, J. Ø.; Wilsgaard, T.; Veyhe, A. S.; Sandanger, T. M. Levels of organochlorines and lipids across pregnancy, delivery and postpartum periods in women from Northern Norway. *J. Environ. Monit.* **2010**, *12*, 2128-2137; DOI: 10.1039/c0em00346h

Hansen, S.; Nieboer, E.; Bravo, N.; Øklandd, I.; Matioceviche, S.; Alvarez, M.V.; Nilseng, S.T.; Grimalt, J.O.; Odland, J.Ø. Variations in serum concentrations of selected organochlorines among delivering women in the northwestern and the southernmost areas of Argentina. The EMASAR. *Study. Environ. Sci.: Proc. Imp.*, submitted

Hites, R. A. Polybrominated diphenyl ethers in the environment and in people: A meta-analysis of concentrations. *Environ. Sci. Technol.* **2004**, *38*, 945–956; DOI 10.1021/es035082g

Jaacks, L. M.; Barr, D. B.; Sundaram, R.; Grewal, J.; Zhang, C.; Buck Louis, G. M. Pre-pregnancy maternal exposure to persistent organic pollutants and gestational weight gain: A prospective cohort study. *Environ. Res. Publ. Health*, **2016**, *13*, 905-916; DOI: 10.3390/ijerph13090905

James, R. A.; Hertz-Picciotto, I.; Willman, E.; Keller, J. A.; Charles, M. J. Determinants of serum polychlorinated biphenyls and organochlorine pesticides measured in women from the child health and development study cohort, 1963-1967. *Environ. Health Perspect.* **2002**, 110, 617-624

Jin, J.; Wang, Y.; Yang, C.; Hu, J.; Liu, W.; Cui, J.; Tang, X. Polybrominated diphenyl ethers in the serum and breast milk of the resident population from production area, China. *Environ. Int.* **2009**, 35, 1048–1052.

Johnson-Restrepo, B.; Kannan, K.; Addink, R.; Adams, D. H. Polybrominated diphenyl ethers and polychlorinated biphenyls in a marine foodweb of coastal Florida. *Environ. Sci. Technol.* **2005**, *39*, 8243-8250; DOI 10.1021/es051551y

Jones-Otazo, H. A.; Clarke, J. P.; Diamond, M. L.; Archbold, J. A.; Ferguson, G.; Harner, T.; Richardson, G. M.; Ryan, J. J.; Wilford, B. Is house dust the missing exposure pathway for PBDEs? An analysis of the urban fate and human exposure to PBDEs. *Environ. Sci. Technol.* **2005**, *39*, 5121-5130; DOI: 10.1021/es048267b

Junqué, E.; Garí, M.; Arce, A.; Torrent, M.; Sunyer, J.; Grimalt, J.O. Integrated assessment of infant exposure to persistent organic pollutants and mercury via dietary intake in a central western Mediterranean site (Menorca Island). Environ. Res. **2017,** 156, 714-724.

Llobet, J. M.; Bocio, A.; Domingo, J. L.; Teixidó, A.; Casas, C.; Müller, L. Levels of polychlorinated biphenyls in foods from Catalonia, Spain: Estimated dietary intake. *J. Food Protect.* **2003**, *3*, 355-521

Llop, S.; Murcia, M.; Alvarez-Pedrerol, M.; Grimalt, J. O.; Santa Marina, L.; Julvez, J.; Goñi-Irigoyen, F.; Espada, M.; Ballester, F.; Rebagliato, M.; Lopez-Espinosa, M. J. Association between exposure to organochlorine compounds and maternal thyroid status: Role of the iodothyronine deiodinase 1 gene. Environ. Int. **2017,** 104, 83-90.

Longnecker, M. P.; Klebanoff, M. A.; Zhou, H.; Brock, J. W. Association between maternal serum concentration of the DDT metabolite DDE and preterm and small-for-gestational-age babies at birth. *Lancet*, **2001**, *358*, 110-114

López-Espinosa, M. J.; Vizcaino, E.; Murcia, M.; Llop, S.; Espada, M.; Seco, V.; Marco, A.; Rebagliato, M.; Grimalt, J. O.; Ballester, F. Association between thyroid hormone levels and 4,4'-DDE concentrations in pregnant women (Valencia, Spain). *Environ. Res.*, **2009**, *109*, 479-485; DOI: 10.1016/j.envres.2009.02.003

Lopez-Espinosa, M. J.; Costa, O.; Vizcaino, E.; Murcia, M.; Fernandez-Somoano, A.; Iñiguez, C.; Llop, S.; Grimalt, J. O.; Ballester, F.; Tardon, A. Prenatal exposure to polybrominated flame retardants and fetal growth in the INMA cohort (Spain). Env. Sci. Technol. **2015,** 49, 10108-10116.

López-Espinosa, M. J.; Murcia, M.; Iniguez, C.; Vizcaíno, E.; Costa, O.; Fernández-Somoano, A.; Basterrechea, M.; Lertxundi, A.; Guxens, M.; Gascón, M.; Goñi-Irigoyen, F.; Grimalt, J. O.; Tardón, A.; Ballester, F. Organochlorine compounds and ultrasound measurements of fetal growth in the INMA Cohort (Spain). *Environ. Health Perspec.*, **2016**, *124*, 157-163; DOI: 10.1289/ehp.1408907

Luchini, L.; Wicki, G.A. Evaluación del potencial para acuicultura en la Provincia de Tierra del Fuego. Información Básica. 2002 (revisión). Secretaría de Agricultura, Ganadería, Pesca y Alimentos (SAGPyA). 29pp.

Manaca, M. N.; Grimalt, J. O.; Sunyer, J.; Mandomando, I.; Gonzalez, R.; Sacarlal, J.; Dobaño, C.; Alonso, P. L.; Menendez, C. Concentration of DDT compounds in breast milk from African women (Manhiça, Mozambique) at the early stages of domestic indoor spraying with this insecticide. *Chemosphere* **2011**, 85, 307-314.

Manaca, M. N.; Grimalt, J. O.; Sunyer, J.; Guinovart, C.; Sacarlal, J.; Menendez, C.; Alonso, P. L.; Dobaño, C. Population characteristics of young African women influencing prenatal exposure to DDT (Manhiça, Mozambique). Environ. Sci. Pollut. Res. **2013**, 20, 3472-3479.

Martí-Cid, R.; Bocio, A.; Llobet, J. M.; Domingo, J. L. Intake of chemical contaminants through fish and seafood consumption by children of Catalonia, Spain: Health risks. *Food Toxicol.* **2007**, *45*, 1968-1974; DOI 10.1016/j.fct.2007.04.014

Morales, E.; Bustamante, M.; Vilahur, N.; Escaranis, G.; Montfort, M.; de Cid, R.; Garcia-Esteban, R.; Torrent, M.; Estivill, X.; Grimalt, J. O.; Sunyer, J. DNA hypomethylation at ALOX12 is associated with persistent wheezing in childhood. Am. J. Respir. Crit. Care Med. **2012,** 185, 937-943.

Morales, E.; Gascon, M.; Martinez, D.; Casas, M.; Ballester, F.; Rodriguez-Bernal, C. L.; Ibarluzea, J.; Santa Marina, L.; Espada, M.; Goñi, F.; Vizcaino, E.; Grimalt, J. O.; Sunyer, J. Associations between blood persistent organic pollutants and 25-hydroxyvitamin D3 in pregnancy. Environ. Int. **2013,** 57-58, 34-41.

Morales, E.; Sunyer, J.; Castro-Giner, F.; Estivill, X.; Julvez, J.; Ribas-Fitó, N.; Torrent, M.; Grimalt, J. O., de Cid, R. Influence of glutathione S-transferase polymorphisms on cognitive functioning effects induced by p,p´-DDT among preschoolers. *Environ. Health Perspect.* **2008**, 116, 1581-1585.

Nøst, T. H.; Breivik, K.; Fuskevåg, O. M.; Nieboer, E.; Odland, J. Ø.; Sandanger, T. M. Persistent organic pollutants in Norwegian men from 1979 to 2007: intraindividual changes, age-period-cohort effects, and model predictions. *Environ. Health Perspect.* **2013**, *121*, 1292-1298; DOI: 10.1289/ehp.1206317

Økland, I.; Odland, J.Ø; Matiocevich, S.; Alvarez, M.V.; Aarsland, T.; Nieboer, E.; Hansen, S. The Argentinian Mother-and-Child Contaminant Study: a cross-sectional study among delivering women in the cities of Ushuaia and Salta. *Study. Environ. Sci.: Proc. Imp.*, submitted

Olsen, J. Prenatal exposures and long term health effects. *Epidemiol. Rev.* **2000**, *22*, 76-81

Palou-Serra, A.; Murcia, M.; Lopez-Espinosa, M. J.; Grimalt, J. O.; Rodriguez-Farre, E.; Ballester, F.; Suñol, C. Influence of prenatal exposure to environmental pollutants on human cord blood levels of glutamate. Neurotoxicol. **2104,** 40, 102-110.

Perelló, G.; Díaz-Ferrero, J.; Llobet, J. M.; Castell, M.; Vicente, E.; Nadal, M; Domingo, J. L. Human exposure to PCDD/Fs and PCBs through consumption on fish and seafood in Catalonia (Spain): Temporal trend. *Food Chem. Toxicol.* **2015**, *81*, 28-33; DOI: 10.1016/j.fct.2015.04.010

Phillips, D. L.; Pirkle, J. L.; Burse, V. W.; Bernert, J.T.; Henderson, L. O.; Needham, L. L. Chlorinated hydrocarbon levels in human serum: effects of fasting and feeding. *Arch. Environ. Contam. Toxicol.* **1989**, *18*, 495-500

Polder, A.; Skaare, J. U.; Skjerve, E.; Løken, K. B.; Eggesbø, M. Levels of chlorinated pesticides and polychlorinated biphenyls in Norwegian breast milk (2002-2006), and factors that may predict the level of contamination. *Sci. total Environ.* **2009**, 407, 4584-4590; DOI: 10.1016/j.scitotenv.2009.04.032

Porta, M.; Gasull, M.; Puigdomènech, E.; Garí, M.; Bosch de Basea, M.; Guillén, M.; López, T.; Bigas, E.; Pumarega, J.; Llebaria, X.; Grimalt, J. O.; Tresserras, R. Distribution of blood concentrations of persistent organic pollutants in a representative sample of the population of Catalonia. *Environ. Int.* **2010**, 36, 655-664.

Rasmussen, K. M.; Catalano, P. M.; Yaktine, A. L. New guidelines for weight gain during pregnancy: what obstetrician/gynecologists should know. Curr Opin Obstet Gynecol. 2009, 21(6), 521–526

Ribas-Fito, N.; Torrent, M.; Carrizo, D.; Muñoz-Ortiz, L.; Julvez, J.; Grimalt, J. O.; Sunyer, J. In Utero Exposure to Background Concentrations of DDT and Cognitive Functioning among Preschoolers. *Am. J. Epidemiol.* **2006**, 164, 955-962.

Rudge, C.V.C; Sandanger, T.; Röllin, H.B.; Calderon, I.M.P.; Volpato, G.; Silva, J.L.P.; Duarte, G.; Neto, C.M.; Sass, N.; Nakamura, M.U.; Odland, J.Ø.; Rudge, M.V.C. Levels of selected persistent orgànic pollutants in blood from delivering women in seven selected areas of São Paulo State, Brazil, *Environ. Intern.* **2012**, 40, 162-169. DOI: 10.1016/j.envint.2011.07.006

Sandanger, T. M.; Sinotte, M.; Dumas, P.; Marchand, M.; Sandau, C. D.; Pereg, D.; Bérubé, S.; Brisson, J.; Ayotte, P. Plasma concentrations of selected organobromine compounds and polychlorinated biphenyls in postmenopausal women of Québec, Canada. *Environ. Health Perspect.* **2007**, 115, 1429–1434.

Schade, G., Heinzow, B. Organochlorine pesticides and polychlorinated bi-phenyls in human milk of mothers líving in northern Germany: corrent extent of contamination, time trend from 1986 to 1997 and factors that influence the levels of contamination. Sci. Total. Environ. **1998**, 215, 31–39.

Simonich, S. L.; Hites, R. A. Global distribution of persistent organochlorine compounds. *Science* **1995**, *269*, 1851-1854

Valvi, D.; Mendez, M. A.; Garcia-Esteban, R.; Ballester, F.; Ibarluzea, J.; Goñi, F.; Grimalt, J. O.; Llop, S.; Marina, L. S.; Vizcaino, E.; Sunyer, J.; Vrijheid, M. Prenatal exposure to persistent organic pollutants and rapid weight gain and overweight in infancy. *Obesity* **2014**, *22*, 488-496; DOI: 10.1002/oby.20603

Valvi, D.; Mendez, M. A.; Martinez, D.; Grimalt, J. O.; Torrent, M.; Sunyer, J.; Vrijheid, M. Prenatal concentrations of polychlorinated biphenyls, DDE, and DDT and overweight in children. A prospective birth cohort study. Environ. Health Perspect. **2012,** 120, 451-457.

Veyhe, A. S.; Hofoss, D.; Hansen, S.; Thomassen, Y.; Sandanger, T. M.; Odland, J. Ø.; Nieboer, E. The Northern Norway Mother-and-Child Contaminant Cohort (MISA) Study: PCA analyses of environmental contaminants in maternal sera and dietary intake in early pregnancy. *Int. J. Hyg. Environ. Health.* **2015**, *218*, 254-264; doi: 10.1016/j.ijheh.2014.12.001

Vizcaíno, E.; Arellano, L.; Fernández, P.; Grimalt, J. O. Analysis of whole congener mixtures of polybromodiphenyl ethers by gas chromatography-mass spectrometry in both environmental and biological samples at femtogram levels. *J. Chromatogr. A* **2009**, *1216*, 5045-5051; DOI: 10.1016/j.chroma.2009.04.049

Vizcaino, E.; Grimalt, J. O.; Lopez-Espinosa, M.-J.; Llop, S.; Rebagliato, M.; Ballester, F. Maternal origin and other determinants of cord serum organochlorine compound concentrations in infants from the general population. Environ. Sci. Technol. **2010**, 44, 6488-6495.

Vizcaíno, E.; Grimalt, J. O.; Fernández-Somoano, A.; Tardón, A. Transport of persistent orgànic pollutants across the human placenta. *Environ. Int.* **2014a**, *65*, 107-115; DOI: 10.1016/j.envint.2014.01.004

Vizcaíno, E.; Grimalt, J.O.; Glomstad, B.; Fernández-Somoano, A.; Tardón, A. Gestational weight gain and exposure of newborns to persistent organic pollutants. *Environ. Health Perspect.* **2014b**, *122*, 873-879, DOI: 10.1289/ehp.1306758

Weiss, J.; Wallin, E.; Axmon, A.; Jönsson, B. A. G.; Akesson, H.; Janák, K.; Hagmar, L.; Bergman, A. Hydroxy-PCBs, PBDEs, and HBCDDs in Serum from an Elderly Population of Swedish Fishermen's Wives and Associations with Bone Density. Environ. Sci. Technol. **2006**, 40, 6282-6289.

Wenning, R. J.; Martello, L.B. Levels and trends of dioxins, PCBs, and other POPs in abiotic compartments. In *Dioxin and Related Compounds*; Alaee, M.; Springer International Publishing: Switzerland

Wigle, D. T.; Arbuckle, T. E.; Turner, M. C.; Bérubé, A.; Yang, Q.; Liu, S.; Krewski, D. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. *J. Toxicol. Environ. Health B* **2008**, *11*, 373-517; DOI: 10.1080/10937400801921320

Wilson, J.; Berntsen, H. F.; Zimmer, K. E.; Verhaegen, S.; Frizzell, C.; Ropstad, E.; Connolly, L. Do persistent organic pollutants interact with the stress response? Individual compounds, and their mixtures, interaction with the glucocorticoid receptor. *Toxicol. Lett.* **2016**, *241*, 121-132; DOI: 10.1016/j.toxlet.2015.11.014

Zota, A. R.; Rudel, R. A.; Morello-Frosch, R. A.; Brody, J. G. Elevated house dust and serum concentrations of PBDEs in California: unintended consequences of furniture flammability standards? Environ. Sci. Technol. **2008**, 42, 8158–8164.

Table 1. Socio-demographic characteristics of studied populations in Argentina (n = 698).

	Ushuaia - n(%)	Salta - n(%)	p-value[3]
All participants	200 (100)	498 (100)	
Age (years)			<0.01
<25	53 (27)	278 (56)	
25-29	56 (29)	111 (22)	
30-34	46 (24)	58 (12)	
≥35	40 (20)	48 (10)	
Postpartum body mass index			<0.01
Normal weight (<25 kg/m^2)	41 (20)	219 (45)	
Overweight (25-30 kg/m^2)	99 (50)	181 (37)	
Obese (≥30 kg/m^2)	60 (30)	89 (18)	
Parity[1]			<0.01
1	82 (41)	221 (44)	
2	75 (37)	120 (24)	
3	33 (17)	78 (16)	
≥4	10 (5)	78 (16)	
Gestational weight gain[2]			<0.01
Low	17 (9)	157 (36)	
Recommended	25 (13)	104 (24)	
High	150 (78)	180 (41)	
Residence			0.091
Urban	183 (91)	429 (86)	
Semi-urban and rural	15 (8)	36 (7)	

[1]Current alive children + stillborn after week 23; [2]GWG groups are based on the IOM recommendations.[3]p-value from X^2 (Chi-square) t-test

Table 2. Serum POP concentrations (ng/g lipid) in the population of study

	Ushuaia (n=199)							Salta (n=471)						
	%>LOD[a]	GM(95%CI)[b]	Min	50th	90th	Max	50th[c]	%>LOD[a]	GM(95%CI)[b]	Min	50th	90th	Max	50th[c]
HCB	81	8.7(7.6-10)	1.2	8.3	25	448	0.067	58	5.2 (4.8-5.6)	1.2	5.8	15	86	0.043
α-HCH	87	3.9(3.3-4.4)	0.39	4.1	14	56	0.032	32	1.1 (0.99-1.3)	0.25	0.51	14	38	0.0030
β-HCH	62	5.1(4.0-6.5)	0.40	6.8	48	258	0.57	70	7.8 (6.6-9.1)	0.42	11	65	408	0.074
4,4'-DDE	99	33(28-39)	0.89	27	146	20547	0.22	100	67 (59-75)	2.9	58	371	10677	0.42
4,4'-DDT	90	2.7(2.4-3.2)	0.25	3.0	7.7	1682	0.022	97	5.7 (5.2-6.2)	0.30	5.2	17	286	0.039
PCB-118	65	2.8(2.4-3.2)	0.37	3.3	11	53	0.025	79	4.8 (4.4-5.3)	0.47	6.1	15	139	0.042
PCB-138	97	5.3(4.6-6.1)	0.094	5.8	14	37	0.046	97	5.3 (4.8-5.8)	0.12	5.9	18	146	0.041
PCB-153	97	7.7(6.9-8.7)	0.40	8.1	20	40	0.064	94	6.8 (6.3-7.4)	0.38	7.3	20	123	0.051
PCB-180	37	1.6(1.4-1.8)	0.29	1.0	6.3	29	0.0055	30	1.6 (1.5-1.7)	0.51	1.0	7.8	53	0.0060
BDE-153	75	1.8(1.7-2.1)	0.31	1.9	4.4	38	0.017	58	1.6 (1.5-1.7)	0.52	1.2	3.8	71	0.0083
BDE-154	35	1.0(0.95-1.1)	0.41	0.87	2.5	6.6	0.0060	30	0.91 (0.88-0.93)	0.51	0.86	1.2	3.8	0.0060
BDE-209	92	8.2(7.3-9.1)	0.65	2.8	15	147	0.068	92	4.1 (3.9-4.4)	1.5	3.5	9.2	27	0.020

[a]% of samples above the limit of detection. [b]GM(95%CI): Geometric mean with 95% confidence intervals. [c]Median in ng/ml.

Table 3. Results of the regression models showing effects of various determinants in blood serum (n = 599).

Compound	Variable	β[ab]	Std. β[b]	P	Compound	Variable	β[a]	Std. β[b]	P
HCB	Age	0.034	0.24	p<0.001	**PCB-138**	Age	0.056	0.36	p<0.001
	BMI[1]	0.0095	0.044	0.30		BMI[1]	-0.015	-0.062	0.15
	Parity	-0.27	-0.39	p<0.001		Parity	-0.23	-0.30	p<0.001
	GWG[2]	-0.020	-0.16	p<0.001		GWG[2]	-0.015	-0.11	p<0.05
	City[3]	0.38	0.19	p<0.001		City[3]	-0.15	-0.065	0.12
	Residence[4]	0.14	0.049	0.21		Residence[4]	-0.13	-0.041	0.29
α-HCH	Age	0.012	0.056	0.27	**PCB-153**	Age	0.046	0.34	p<0.001
	BMI[1]	-0.032	-0.092	p<0.05		BMI[1]	-0.019	-0.094	p<0.05
	Parity	-0.0021	-0.0019	0.97		Parity	-0.19	-0.29	p<0.001
	GWG[2]	0.012	0.064	0.14		GWG[2]	-0.011	-0.096	p<0.05
	City[3]	1.2	0.37	p<0.001		City[3]	-0.034	-0.018	0.68
	Residence[4]	0.25	0.056	0.16		Residence[4]	-0.18	-0.067	0.098
β-HCH	Age	0.078	0.29	p<0.001	**PCB-180**	Age	0.061	0.42	p<0.001
	BMI[1]	0.037	0.090	p<0.05		BMI[1]	-0.027	-0.12	p<0.01
	Parity	-0.61	-0.46	p<0.001		Parity	-0.19	-0.27	p<0.001
	GWG[2]	-0.025	-0.11	p<0.05		GWG[2]	-0.0076	-0.061	0.18
	City[3]	-0.83	-0.21	p<0.001		City[3]	-0.026	-0.012	0.087
	Residence[4]	0.41	0.075	0.058		Residence[4]	-0.29	-0.10	p<0.05
4,4'-DDE	Age	0.071	0.36	p<0.001	**PBDE-153**	Age	-0.011	-0.10	0.069
	BMI[1]	0.027	0.089	P<0.05		BMI[1]	0.0059	0.035	0.46
	Parity	-0.46	-0.47	p<0.001		Parity	0.030	0.056	0.29
	GWG[2]	-0.012	-0.071	0.085		GWG[2]	-0.012	-0.012	0.79
	City[3]	-1.1	-0.38	p<0.001		City[3]	0.18	0.11	p<0.05
	Residence[4]	0.59	0.15	p<0.001		Residence[4]	-0.047	-0.021	0.62
4,4'-DDT	Age	0.023	0.15	p<0.01	**PBDE-154**	Age	-0.0040	-0.072	0.19
	BMI[1]	0.027	0.11	p<0.01		BMI[1]	-0.0039	-0.045	0.34
	Parity	-0.12	-0.15	p<0.01		Parity	0.0015	0.0054	0.92
	GWG[2]	-0.014	-0.11	p<0.05		GWG[2]	0.0031	0.063	0.18
	City[3]	-0.83	-0.37	p<0.001		City[3]	0.11	0.14	p<0.01
	Residence[4]	0.36	0.11	p<0.01		Residence[4]	-0.015	-0.013	0.76
PCB-118	Age	0.022	0.13	p<0.01	**PBDE-209**	Age	0.00013	0.0011	0.98
	BMI[1]	0.018	0.072	0.11		BMI[1]	-0.0088	-0.051	0.23
	Parity	-0.15	-0.19	p<0.001		Parity	0.018	0.034	0.48
	GWG[2]	-0.021	-0.15	p<0.01		GWG[2]	0.00082	0.0085	0.84
	City[3]	-0.60	-0.25	p<0.001		City[3]	0.68	0.43	p<0.001
	Residence[4]	-0.12	-0.037	0.37		Residence[4]	0.12	0.054	0.17

[a]β coefficients of the multivariate regression models with non-standardized variables. [b]β coefficients of the multivariate regression models after standardizing all the variables.

[1]BMI: Body mass index; [2]GWG: Gestational weight gain; [3]Salta as the reference city; [4]Urban as reference category for residence

FIGURE CAPTIONS

Figure 1. Geometric means of the organohalogen concentrations in postpartum mothers from Salta and Ushuaia (ng/g lipid). The vertical bars plot the 95% confidence interval.

Figure 2. Socio-demographic plots of the geometric means and the 95% confidence intervals (ng/g lipid) of the of the organohalogen compound concentrations in postpartum mothers.

Figure 3. Relative change (%) in median serum organohalogen concentrations by unit change calculated from the β coefficients and standard errors of the multiregression analysis described in Table 3. The units of changes for each variable were set as the difference between the first and third quartile.