



# 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  $\beta$ -hexachlorocyclohexane ( $\beta$ -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  $\beta$ -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  $\alpha$ -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,  $\beta$ -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,  $\beta$ -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,  $\alpha$ -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  $\alpha$ -HCH and the PCB congeners indicated higher dilution at higher weight increase.

## 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., 2015), and infants come to life with an initial POP burden.

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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-Fitó 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 (Gascón 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  $\beta$ -isomer of hexachlorocyclohexane ( $\beta$ -HCH), 4,4'-dichlorodiphenyltrichloroethane (4,4'-DDT) and its main metabolite 4,4'-dichlorodiphenyldichloroethylene (4,4'-DDE) and polychlorinated biphenyls (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 and Martello, 2016; 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  $36 \pm 12$  h 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 subtraction 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/ $\mu$ L). POP extraction was performed by addition of *n*-hexane (2 mL) and H<sub>2</sub>SO<sub>4</sub> (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<sub>2</sub>SO<sub>4</sub>. 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<sub>2</sub>SO<sub>4</sub> (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  $\mu$ L rinses of isooctane which were then reduced to dryness under a very gentle stream of nitrogen. Finally, they were dissolved with 100  $\mu$ L of PCB-142 (internal standard) in isooctane (10 pg/ $\mu$ L). 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  $\mu$ L of [<sup>3-13</sup>C] BDE-209 (6.5 pg/ $\mu$ L) and 30  $\mu$ L of BDE-118 (20 pg/ $\mu$ L) as internal standards (Vizcaino et al., 2009).

### 2.3. Analytical procedure

Nineteen organochlorine compounds (OCs), pentachlorobenzene (PeCB), HCB,  $\alpha$ -HCH,  $\beta$ -HCH,  $\gamma$ -HCH,  $\delta$ -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  $\mu$ m film thickness; JW Scientific) protected with a retention gap. 2  $\mu$ L 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  $\mu\text{m}$  film thicknesses; DB-5MS) protected with a retention gap. One  $\mu\text{L}$  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,  $\alpha$ -HCH,  $\beta$ -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) =  $2.27 \cdot \text{TC} + \text{Tg} + 0.623$ ; Phillips et al., 1989).

Geometric means (GM) and 95% confidence intervals (CI) were used

for descriptive analysis (Fig. 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  $\beta$  coefficients and the standardized  $\beta$  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:  $\log(\text{POP}) = \beta_1(\text{Age}) + \beta_2(\text{BMI}) + \beta_3(\text{Parity}) + \beta_4(\text{GWG}) + \beta_5(\text{Residence}) + \beta_6(\text{City}) + \epsilon$ . 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  $\beta$  coefficients were transformed into relative changes (%) for better representation (Fig. 3). For each variable, median serum concentrations by unit change (c) were calculated as  $(\exp(c \cdot \beta) - 1) \cdot 100$  and the corresponding confidence intervals were calculated as  $(\exp(c \cdot \beta \pm z_{1-\alpha/2} \cdot \text{SE}(\beta)) - 1) \cdot 100$ , using  $\beta$  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 (Figs. 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 ( $16.4 \text{ kg/m}^2$ ) to obesity ( $44.1 \text{ kg/m}^2$ ). 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

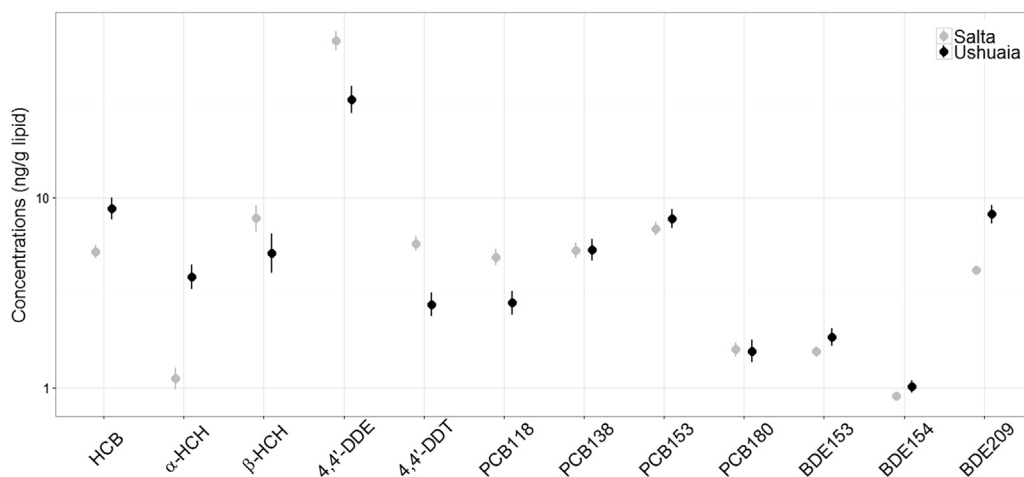


Fig. 1. Geometric means of the organohalogen concentrations in postpartum mothers from Salta and Ushuaia (ng/g lipid). The vertical bars plot the 95% confidence interval.

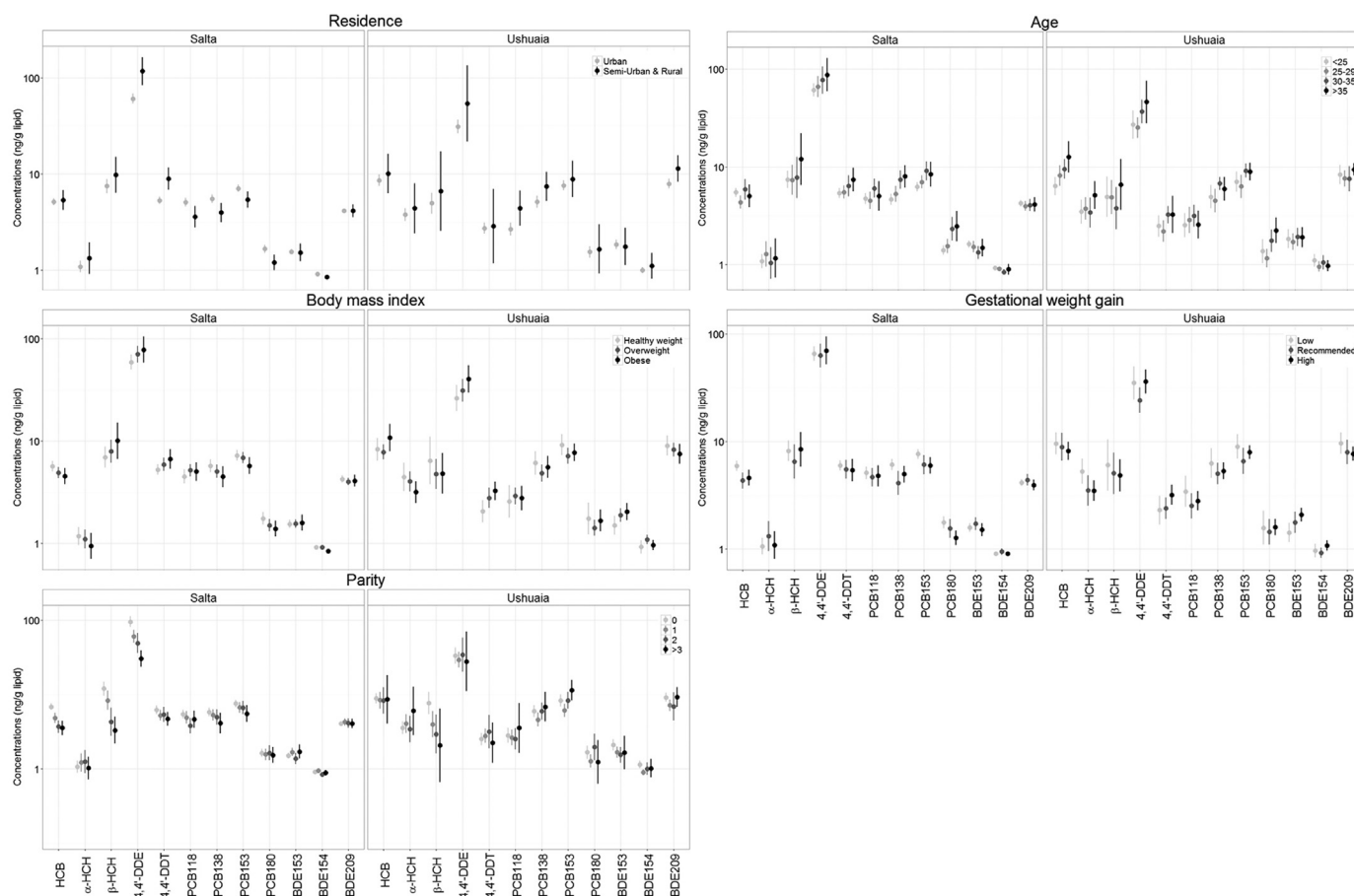


Fig. 2. Socio-demographic plots of the geometric means and the 95% confidence intervals (ng/g lipid) of the of the organohalogen compound concentrations in postpartum mothers.

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

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

<sup>1</sup> Current alive children + stillborn after week 23.  
<sup>2</sup> GWG groups are based on the IOM recommendations.  
<sup>3</sup> p-value from  $\chi^2$  (Chi-square) t-test.

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, Fig. 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

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

	Ushuaia (n = 199)							Salta (n = 471)						
	% > LOD <sup>a</sup>	GM (95%CI) <sup>b</sup>	Min	50th	90th	Max	50th <sup>c</sup>	% > LOD <sup>a</sup>	GM (95%CI) <sup>b</sup>	Min	50th	90th	Max	50th <sup>c</sup>
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	20,547	0.22	100	67 (59–75)	2.9	58	371	10,677	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

<sup>a</sup> % of samples above the limit of detection.  
<sup>b</sup> GM(95%CI): Geometric mean with 95% confidence intervals.  
<sup>c</sup> Median in ng/mL.

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

Compound	Variable	β <sup>a,b</sup>	Std. β <sup>b</sup>	P	Compound	Variable	β <sup>a</sup>	Std. β <sup>b</sup>	P
HCB	Age	0.034	0.24	p < 0.001	PCB-138	Age	0.056	0.36	p < 0.001
	BMI <sup>1</sup>	0.0095	0.044	0.30		BMI <sup>1</sup>	- 0.015	- 0.062	0.15
	Parity	- 0.27	- 0.39	p < 0.001		Parity	- 0.23	- 0.30	p < 0.001
	GWG <sup>2</sup>	- 0.020	- 0.16	p < 0.001		GWG <sup>2</sup>	- 0.015	- 0.11	p < 0.05
	City <sup>3</sup>	0.38	0.19	p < 0.001		City <sup>3</sup>	- 0.15	- 0.065	0.12
	Residence <sup>4</sup>	0.14	0.049	0.21		Residence <sup>4</sup>	- 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 <sup>1</sup>	- 0.032	- 0.092	p < 0.05		BMI <sup>1</sup>	- 0.019	- 0.094	p < 0.05
	Parity	- 0.0021	- 0.0019	0.97		Parity	- 0.19	- 0.29	p < 0.001
	GWG <sup>2</sup>	0.012	0.064	0.14		GWG <sup>2</sup>	- 0.011	- 0.096	p < 0.05
	City <sup>3</sup>	1.2	0.37	p < 0.001		City <sup>3</sup>	- 0.034	- 0.018	0.68
	Residence <sup>4</sup>	0.25	0.056	0.16		Residence <sup>4</sup>	- 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 <sup>1</sup>	0.037	0.090	p < 0.05		BMI <sup>1</sup>	- 0.027	- 0.12	p < 0.01
	Parity	- 0.61	- 0.46	p < 0.001		Parity	- 0.19	- 0.27	p < 0.001
	GWG <sup>2</sup>	- 0.025	- 0.11	p < 0.05		GWG <sup>2</sup>	- 0.0076	- 0.061	0.18
	City <sup>3</sup>	- 0.83	- 0.21	p < 0.001		City <sup>3</sup>	- 0.026	- 0.012	0.087
	Residence <sup>4</sup>	0.41	0.075	0.058		Residence <sup>4</sup>	- 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 <sup>1</sup>	0.027	0.089	P < 0.05		BMI <sup>1</sup>	0.0059	0.035	0.46
	Parity	- 0.46	- 0.47	p < 0.001		Parity	0.030	0.056	0.29
	GWG <sup>2</sup>	- 0.012	- 0.071	0.085		GWG <sup>2</sup>	- 0.012	- 0.012	0.79
	City <sup>3</sup>	- 1.1	- 0.38	p < 0.001		City <sup>3</sup>	0.18	0.11	p < 0.05
	Residence <sup>4</sup>	0.59	0.15	p < 0.001		Residence <sup>4</sup>	- 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 <sup>1</sup>	0.027	0.11	p < 0.01		BMI <sup>1</sup>	- 0.0039	- 0.045	0.34
	Parity	- 0.12	- 0.15	p < 0.01		Parity	0.0015	0.0054	0.92
	GWG <sup>2</sup>	- 0.014	- 0.11	p < 0.05		GWG <sup>2</sup>	0.0031	0.063	0.18
	City <sup>3</sup>	- 0.83	- 0.37	p < 0.001		City <sup>3</sup>	0.11	0.14	p < 0.01
	Residence <sup>4</sup>	0.36	0.11	p < 0.01		Residence <sup>4</sup>	- 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 <sup>1</sup>	0.018	0.072	0.11		BMI <sup>1</sup>	- 0.0088	- 0.051	0.23
	Parity	- 0.15	- 0.19	p < 0.001		Parity	0.018	0.034	0.48
	GWG <sup>2</sup>	- 0.021	- 0.15	p < 0.01		GWG <sup>2</sup>	0.00082	0.0085	0.84
	City <sup>3</sup>	- 0.60	- 0.25	p < 0.001		City <sup>3</sup>	0.68	0.43	p < 0.001
	Residence <sup>4</sup>	- 0.12	- 0.037	0.37		Residence <sup>4</sup>	0.12	0.054	0.17

<sup>a</sup> β Coefficients of the multivariate regression models with non-standardized variables.  
<sup>b</sup> β coefficients of the multivariate regression models after standardizing all the variables.  
<sup>1</sup> BMI: Body mass index.  
<sup>2</sup> GWG: Gestational weight gain.  
<sup>3</sup> Salta as the reference city.  
<sup>4</sup> Urban as reference category for residence.

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 Fig. 1). The concentrations of DDT compounds in the

mothers from the former city were two times higher than those in the second (Table 2, Fig. 1) which may reflect much stronger use of organochlorine pesticides in relation to past agricultural activities. Conversely, the mothers from Ushuaia showed significant higher concentrations of HCB (p < 0.001), α-HCH (p < 0.001), BDE congeners

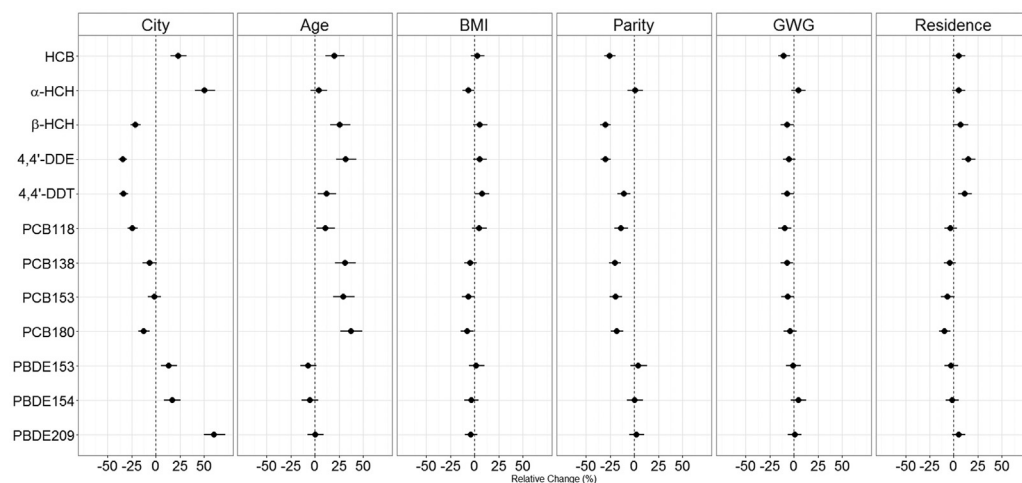


Fig. 3. Relative change (%) in median serum organohalogen concentrations by unit change calculated from the  $\beta$  coefficients and standard errors of the multi-regression analysis described in Table 3. The units of changes for each variable were set as the difference between the first and third quartile.

153 ( $p < 0.05$ ), 154 ( $p < 0.01$ ) and 209 ( $p < 0.001$ ). The concentrations of  $\alpha$ -HCH and BDE congener 209 in the former were two times or higher than those in the latter (Table 2, Fig. 2). The most volatile compounds in this study, HCB and  $\alpha$ -HCH, were mainly found in Ushuaia (Fig. 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, Fig. 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 (Fig. 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 (Fig. 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 (Fig. 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 (Fig. 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 (Fig. 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  $\alpha$ -HCH (Table 3). This trend was clearly observed in Salta and to a lower extent in Ushuaia. (Fig. 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  $\alpha$ -HCH and PCB congeners 153 and 180 (Fig. 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 (Fig. 2) which were those related with agricultural activities. In contrast, the reverse correlations of  $\alpha$ -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 (Garí and Grimalt, 2013) or post-menopausal 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 Monterey 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, 2015). 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 (Fig. 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., 2014a, 2014b).

### 3.8. Multiregression analysis

Linear and non-linear multivariate models of the aforementioned variables (Table 3, Fig. 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,  $\alpha$ -HCH and PBDEs in Ushuaia and higher concentrations of  $\beta$ -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  $\beta$ -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 (Fig. 3). Parity was the main second determinant of HCB,  $\beta$ -HCH, 4,4'-DDT and PCB congener 118 (Fig. 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,  $\beta$ -HCH, 4,4'-DDT and PCB congeners 118, 138 and 153. BMI was also a determinant for PCB congeners 153 and 180,  $\alpha$ -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  $\beta$ -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,  $\alpha$ -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  $\alpha$ -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  $\alpha$ -HCH, were found in higher concentration in the colder area (Ushuaia).

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## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.envres.2017.07.033>.

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