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Placental levels of metals and associated factors in urban and sub-urban areas of Seville (Spain)

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ABSTRACT

Environmental exposure to metals among women, revealed their adverse effects on pregnancy. The fetus is exposed to these toxic elements only via the placenta which are able to accumulate there or cross it, compromising the protective functions of this organ. Numerous studies have shown associations between the prenatal exposition to some metals and an impact on cognitive, motor and intellectual development of the child. Sixty two placental samples were taken at delivery to determine the mineral content (Al, B, Ba, Ca, Cd, Cr, Cu, Fe, K, Li, Mg, Mn, Mo, Na, Ni, Pb, Sr, V, Zn) by ICP-OES. Among these metals, essential ones (B, Ca, Cu, Fe, Mg, Mn, Mo, Na, Zn) can have health beneficial effects at low levels however, in high concentration are potentially toxic. On the other hand, elements such as Al, Cd, Pb, are classified as toxic metals, no matter what its concentration is. The aim of this study is to find the potential relationships between these metals levels, newborn's parameters, pregnancy details and the epidemiologic information obtained using a questionnaire data from the participant pregnant women from Seville (Spain).

The main maternal determinant of detectable placenta Cd levels was smoking during pregnancy. Other maternal factors that may affect placenta metal levels were gestational age (Al, B, Ba, and Pb) or dietary supplement (Fe). It has to be stressed that our results have to be interpreted with caution, because of the small study group and the low exposure levels, along with the lack of information on potential sources of exposure to these metals. The use of placenta samples obtained at delivery can be considered strength of this study since the concentration of some metals in placenta can indicate the extent of maternal exposure during gestation.

1. Introduction

Pregnant women are exposed to a wide variety of foreign chemicals through their diet, maternal medication, lifestyle factors, such as smoking, drug abuse, and alcohol consumption, or occupational and environmental sources [1]. Prenatal period is considered to be the most sensitive phase in human development. During this time fetal cells are the subjects of division and differentiation. This is the reason of high susceptibility of fetus to neurotoxic stressors which can easily cause developmental alterations [2]. The fetus is exposed to these toxic contaminants only via the placenta. When substances reach the placenta they can be metabolized and accumulated, thus acting as an efficient or partially protective barrier [3] or cross it by passive diffusion or by active transport, pinocytosis or filtration. Some lipophilic compounds of low molecular weight are able to cross the placenta without restriction and may impact physiological transport mechanisms, compromising the protective functions of this organ [4,5]. Placental tissue is considered as non-invasive exposure biomarker for different organic and inorganic pollutants. Thus, Cd concentrations were 10 times higher than that detected in maternal blood and up to 100 times higher than that of cord blood indicate that Cd accumulates in the placenta during gestation. This tissue usually discarded after birth, is easy to obtain and may reflect the simultaneous exposure status to these contaminants of mothers and their fetus as well as the first lifetime exposure time point of the fetus [3,6].

Heavy metals have been found to have an impact, in particular on

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cognitive, motor and intellectual development after a prenatal exposure [7,8]. Cadmium (Cd), and lead (Pb) are developmental toxicants with no known biological function that are transported across the placenta [7].Thus, has been reported that prenatal exposure to Pb and Cd is associated with reduce birth weight, birth length and head circumference [9]. Also, infertility, spontaneous abortions, and fetal and neonatal death have been reported after either male or female occupational exposure to Pb [10]. Cd exposition is associated mainly with cigarette smoke and its ovarian concentration increases with age, and has been associated with retardation of trophoblastic outgrowth and development, placental necrosis and suppression of steroid biosynthesis, and altered handling of nutrient metals by the placenta all contribute to implantation delay and possible early pregnancy loss [11]. Maternal iron (Fe) status has been a critical factor for pregnancy outcomes because maternal anemia as well as iron deficiency increases the risk of adverse pregnancy outcomes such as preterm delivery and low birth weight [10]. Treatment with Lithium (Li), as well as exposure to the metal via drinking water and other environmental sources, is associated with adverse health outcomes [12].

On the other hand, human organism has requirements of appropriate amounts of essential metals such as K, Ca, Co, Cr, Cu, Mg, Mn, and Zn to maintain optimum health, though outside of beneficial intake ranges, either elevated or reduced levels of these metals can adversely affect health [12,13]. The physiological role of Mn in the developing organism in the animal model is well documented, but little is known about the adverse effects of Mn deficiency or overexposure in the human, including pregnancy outcome and birth weight [14]. Dietary zinc deficiencies also cause developmental problems throughout pregnancy [10].

It is therefore important to assess the nature and degree of exposure in pregnant women because also is the exposure of the unborn child. Many various factors may have a significant influence on the prenatal concentration of toxic metals, e.g. smoking during pregnancy, maternal age, gestational age [15]. It seems to be useful to know about the relationship between the above-specified factors and the concentration of metals in placenta. The aim of the study was the simultaneous determination by ICP-OES of Al, B, Ba, Ca, Cd, Cr, Cu, Fe, K, Li, Mg, Mn, Mo, Na, Ni, Pb, Sr, V, Zn in placental samples taken at delivery to find the potential relationships between these metals concentration, newborn's parameters, pregnancy details and the epidemiologic information obtained using a questionnaire data from the participant pregnant women from Seville (Spain).

2. Material and methods

2.1. Study population

Sixty two healthy women living in Seville, south of Spain, participated in this research study in year 2016. Only women who had been residents in the study area and who were older than 18 years old at the time of delivery were recruited for this study. Women who followed any program of assisted reproduction or who suffered from chronic hypertension, any type of diabetes, thyroid disorders or chronic renal or cardiac disease during pregnancy were excluded. The study was approved by Coordinating Committee for the Ethics of Biomedical Research of Andalusia. The consents were obtained from all the pregnant who agreed to participate in this study and who were admitted.

The samples of placenta were taken just after the delivery in the Department of Genetics, Reproduction and Fetal Medicine in Hospital Virgen del Rocío (Sevilla). Five samples of approximately 5 g each were taken from its four corners and one from the middle. All portions of the samples were about 1 cm in width and length and 0.5 cm thickness. No gross morphological abnormalities were observed. Samples were washed twice in cold PBS, cut into smaller pieces and homogenized. Then the homogenized samples were immediately coded, frozen and stored at -80 °C until analysis. Samples were supported with the newborn's parameters (bodyweight, body length, Apgar score) and sex of the child. Also a detailed questionnaire with demographic, socioeconomic, lifestyle, and environmental data was filled in a face to face interview.

2.2. Chemical and reagents

Panreac (Barcelona, España) standard solutions of about 1000 mg L^{-1} were used as stock solution of each element for calibration. Other reagents used where of analytical grade. Milli-Q treated water was used throughout.

2.3. Analytical procedure

Placental samples with presence of an excess of blood were discarded to avoid the contamination of the placental tissue though the maternal and fetal blood. A portion of 10.2 ± 0.5 g of each homogenized sample was placed in porcelain crucibles that were desiccated for 24 h in an oven at 70 °C. The samples were then subjected to incineration in a muffle furnace with a temperature-time program of 450 ± 25 °C-18 to 24 h, until the production of white ashes which were dissolved in nitric acid 5% to a volume of 50 mL [16]. The final dissolution factor of the sample was 1/5 (m/V) (10 g of sample diluted in 50 ml of acid).

The metals were determined by Inductively Coupled Plasma-Optical Emission Spectrometry (ICP-OES) technique; model ICAP 6300 Duo Thermo Scientific. The instrumental conditions were as follows: approximate RF power, 1150 W; gas flow (nebulizer gas flow, auxiliary gas flow), 0.5 L/min; injection of the sample to the pump flow, 50 rpm; stabilization time, 0 s.

2.4. Quality controls

Detection and quantification limits under reproducibility conditions, which were estimated as three and ten times the standard deviation (SD) resulting from the analysis of 15 blanks [17] were the lowest for Cd and Pb LOD: 0.003 μg/g and LOQ: 0.008 μg/g and the highest for Na: LOD: 9.142 μg/g and LOQ: 30.46 μg/g, Ca: LOD: 4.833 μg/g and LOQ: 16.29 μg/g and K: LOD: 4.708 μg/g and LOQ: 15.70 μg/g.

Quality controls were performed to verify the accuracy of the analytical procedure. These controls were based on the study of the recovery percentage obtained with blank samples and reference material measured under reproducible conditions. Reference materials (SRM 1566b Oyster Tissue, SRM 1573a Tomato Leaves and SRM 1515 Apple Leaves from the National Institute for Standards and Technology (NIST)) were processed by digestion as the same way as placenta samples. The recoveries obtained were all upper than 92%. Along the analytical procedures, each batch of 20 samples was analyzed together with at least a blank and a reference sample. Calibration was performed using the calibration curve method.

2.5. Statistical analysis

Statistical analysis was performed using the statistical package IBM Statistics SPSS 24.0 (Statistical Package for the Social Sciences). To describe the characteristics of our participants, descriptive statistical parameters were initially computed. Arithmetic mean ± standard deviation, geometric mean, minimum and maximum values of concentration above the limit of detection were calculated for potential continuous variables. Categorical variables were described using frequencies and percentages.

Spearman's correlation analysis was conducted to assess relationships between metal concentrations in placenta tissue. Normality of distributions for each continuous variable was assessed with Shapiro-Wilks test; non-parametric Kruskal-Wallis test were performed in bivariate analyses in not normally distributed variables. ANOVAs were

used to compare continuous variables between two groups.

Multiple linear regression models were conducted to examine potential factors contributing to exposure levels, with logarithm-transformed concentrations of the metals as dependent variables. Previously, it was made a selection of the variables that will be introduced in the model by calculating Pearson's linear correlation coefficients. Due to the high number of potentially candidate variables to be introduced in the multiple linear regression models, we applied a previous pre-selection based on bivariate analysis, following the methodology used in all the multivariate techniques of construction of regression models. All covariates were tested in multivariate analysis and only were included in the final model those which were significantly associated with metal levels in prior bivariate analyses ($P \leq 0.1$). The collinearity of the independent variables also was considered by calculating the tolerance and the variance inflation factor.

3. Results and discussion

3.1. Study participants

The age of the mothers at delivery was mainly ranging from 31 to 40 years. Most of the participants were from Spain and just the 42% of all of them resided in the metropolitan area (Seville), with the remaining participants spread across the sub urban area, predominantly around the west of the province of Seville. Only the 45.2% of the participants had tertiary education studies. Only 13% of the women were working during the pregnancy. The majority of participating mothers did not smoke, though the 22.6% of the participants were smoking along the pregnancy. Also it was considered if pregnant took or not supplemental Fe.

Factors potentially connected to metal levels and/or socio-demographic and lifestyle characteristics were also considered. Thus, 92% of participants had not previous premature delivery, neither previous misbirth. The gestational age was 39 ± 1.4 weeks, the mean neonatal weight around 3229 ± 646 g and the apgar score at 10 min was in all the cases 10.

3.2. Profile of metals in placenta

The concentration and descriptive statistics for each metal in placenta are reported in Table 1. No differences were detected in metal levels in placentas from male or female newborn in our study. There are only a few recent studies that have investigated essential elements in human placenta. Our results showed that almost 100% of placenta samples contained quantifiable amounts of alkali and alkaline earth metals, with the exception of Ba and Ca (98 and 95%, respectively). Metalloids and post-transition metals reached 100% of LOQ in placenta tissue. The highest concentration were observed for K (geometric mean: 1185.75 μg/g), Na (geometric mean: 1070.53 μg/g), Ca (geometric mean: 352.59 μg/g) and Mg (geometric mean: 77.94 μg/g). The concentrations of Ca and Al were similar to those seen in singleton pregnant women in Rochester (NY) [5] but levels of Ca was lower when comparing with both fetal and maternal placental from teenagers and adults women from Brazil [18], this differences may be due to dietary patterns. However, levels of Ba, Mg and Sr were 44-fold, 3-fold and 4-fold higher respectively, in comparison with de Angelis et al. [5] study. It should be noted the great difference in Ba levels from the two locations (Rochester vs Seville). Taking into account that this metal is not present in food, the possible explanation may be differences in geographical pollution. Among transition metals Ni and Cr were the elements with the high percentages of samples with concentration below quantification limits (79 and 77%, respectively) followed by Mn and V with a 40% under the LOQ. Concentrations were particularly low for Molybdenum (geometric mean: 9.3 ng/g), Nickel (geometric mean: 35.05 ng/g) and Chromium (geometric mean: 79.59 ng/g) close all of them to its limit of quantification. In spite of this, concentrations of the all transition metals were higher than those detected in singleton pregnant by de Angelis et al. [5]. On the contrary, in comparison with our data, levels of Fe were significantly higher in fetal and maternal placental from women in Brazil [18]. This difference in Fe levels should be due to a deficit in Fe levels in our population, where women even having iron supplements presented lower levels of this metal than those who didn't have it. Kubala-Kukus et al. [19] presented values of Ca, Cu, Fe and Zn in the placentas of women from rural and urban areas of Poland. The respective averages in both areas were higher (4-fold, 1.5-fold, 3-fold and 2-fold, respectively) than those of the present study.

Table 1
Descriptive statistics of the metal concentrations in placenta*. Concentrations are in μg/g unless otherwise noted.

Group & element	N	% > LOD	% > LOQ	Mean ± SD	Geometric Mean	Minimum-maximum
Alkali Metals						
Na	62	100	100	1078.94 ± 128.67	1070.53	580.26-1314.76
K	62	100	100	1205.37 ± 206.12	1185.75	482.32-1643.07
Li	62	100	100	0.47 ± 0.34	0.37	0.03-2.34
Alkaline Earth Metals						
Ba	62	100	98	0.39 ± 0.22	0.34	0.12-1.07
Ca	62	100	95	567.74 ± 697.89	352.60	110.92-2756.31
Mg	62	100	100	77.94 ± 18.42	76.06	54.25-139.70
Sr	62	100	100	0.31 ± 0.25	0.24	0.09-1.06
Metalloids						
B	62	100	100	0.39 ± 0.11	0.37	0.19-0.63
Post transition metals						
Al	62	100	100	4.82 ± 5.73	2.68	0.46-26.37
Pb (ng/g)	62	100	100	41.99 ± 14.80	39.78	23.87-84.60
Transition Elements						
Cd (ng/g)	62	100	94	17.24 ± 12.20	19.92	9.42-72.39
Cr (ng/g)	62	82	23	83.24 ± 28.10	79.59	60.01-144.84
Cu	62	100	100	0.97 ± 0.24	0.94	0.43-1.54
Fe	62	100	100	51.07 ± 13.74	49.14	25.10-81.24
Mn	62	100	60	1.66 ± 9.56	0.11	0.07-58.22
Mo (ng/g)	62	100	94	9.56 ± 2.34	9.30	7.01-15.00
Ni (ng/g)	62	95	21	39.27 ± 23.33	35.05	23.30-109.49
V (ng/g)	62	100	60	72.42 ± 21.71	69.10	40.01-116.26
Zn	62	100	100	8.43 ± 0.97	8.38	6.38-11.27

* Elements are arranged by periodic group.

Table 2
Results of Multiple Linear regression models of factors influencing placenta metals concentrations.

Metal	Factors	Standardized coefficient		95% confidence interval for beta		R^2	Adj. R^2
		Beta	Sig	Lower bound	Upper bound		
Al	Constant	0.253	0.083	−13.960	0.885	0.064	0.049
	Gestational age (weeks)		**0.047**	0.003	0.382		
B	Constant	0.286	0.001	−5.496	−1.454	0.180	0.138
	Gestational age (weeks)	−0.125	**0.023**	0.009	0.110		
	Age	0.245	0.313	−0.218	0.071		
	≤30		0.044	0.004	0.281		
	> 30						
	Medication (yes/no Fe)						
Ba	Constant	0.366	0.000	−9.436	−2.808	0.210	0.183
	Gestational age (weeks)	−0.298	**0.003**	0.048	0.217		
	Vegetable consumption		**0.014**	−0.546	−0.066		
	≤1						
	> 1						
Ca	Constant	0.248	0.719	−7.899	5.487	0.107	0.075
	Gestational age (weeks)	0.223	0.055	−0.004	0.334		
	Medication (yes/no Fe)		0.083	−0.053	0.837		
Cd	Constant	0.228	0.000	−11.362	−3.528	0.095	0.062
	Gestational age (weeks)	−0.156	0.091	−0.014	0.184		
	Age		0.245	−0.410	0.107		
	≤30						
	> 30						
Cr	Constant	−0.525	0.000	−2.563	−1.504	0.276	0.215
	Neonatal weight (g)		0.054	0.000	0.000		
Cu	Constant	−0.243	0.814	−0.091	0.115	0.059	0.043
	Age		0.057	−0.266	0.004		
	≤30						
	> 30						
Fe	Constant	0.226	0.058	−0.062	3.824	0.123	0.093
	Gestational age (weeks)	0.263	0.069	−0.004	0.095		
	Fe supplementation (yes/no)		**0.035**	0.011	0.288		
K	Constant	0.237	0.000	6.878	7.095	0.056	0.040
	Maternal education (yes/no university)		0.064	−0.007	0.234		
Li	Constant	0.214	0.000	−1.824	−0.855	0.046	0.030
	Medication (yes/no Fe)		0.095	−0.048	0.577		
Mg	Constant	0.266	0.000	4.093	4.336	0.071	0.055
	Maternal education (yes/no university)		**0.036**	0.009	0.281		
Mo	Constant	0.219	0.000	−5.043	−4.702	0.101	0.068
	Residence (Seville/other)	0.234	0.095	−0.020	0.241		
	Maternal education (yes/no university)		0.075	−0.015	0.303		
Na	Constant	0.205	0.000	6.742	7.004	0.042	0.026
	Age living in this area (> / < 5 years)		0.109	−0.014	0.133		
Ni	Constant	−0.105	0.000	−3.146	−1.344	0.541	0.457
	Smoking during pregnancy (yes/no)	−0.675	0.670	−0.680	0.454		
	Neonatal weight (g)		**0.017**	−0.534	−0.065		
Pb	Constant	0.275	0.000	−7.931	−3.321	0.118	0.087
	Gestational age (weeks)	−0.148	**0.035**	0.005	0.121		
	Age		0.251	−0.262	0.070		
	≤30						
	> 30						
Sr	Constant	0.213	0.033	−10.083	−0.431	0.113	0.082
	Gestational age (weeks)	−0.216	0.100	−0.020	0.224		
	Age		0.095	−0.645	0.053		
	≤30						
	> 30						
V	Constant	−0.317	0.000	−2.680	−2.267	0.222	0.151
	Vegetable consumption	−0.290	0.113	−0.450	0.051		
	≤1		0.146	−0.436	0.069		
	> 1						
	Water consumption						
	≤1.5 L						
	> 1.5 L						
Zn	Constant	0.211	0.001	0.608	2.157	0.109	0.079
	Gestational age (weeks)	0.251	0.092	−0.003	0.037		
	Fe supplementation (yes/no)		**0.046**	0.001	0.112		

Toxic metals such as Pb, Cd, and Mn and other metals as Cu and Zn were detected in 100% of the participants in comparison with Cr and Ni that were detected in 82% and 95% of the placenta samples. Mean values of Cr and Mn in the present study were in concordance of those reported by Amaya et al. [20] in a Spanish birth cohort. However, Cd levels were 6-fold higher in our study and Pb twice lower. The low prevalence of Pb (35%) observed by Amaya et al. [20] in comparison with the present study (100%) could explain the significant differences between the concentrations detected in both studies. Comparing our results with a more recent Spanish study in seven birth cohorts, it can be observed higher levels in Cd (5-fold higher) Mn (1.5-fold higher) and Pb which it was detected under LOD in with a low detection frequencies

[21]. Similar levels of Mn and Zn were detected by Punshon et al. [7] in comparison with those obtained in the present study; however detected levels of Cd and Pb were higher in our pregnant cohort. This also was observed when comparing our mean placenta Pb, Cd and Zn concentrations with the means reported by Al-Saleh et al. [22] in pregnant women from Riad (Saudi Arabia) and by de Angelis et al. [5] in singleton pregnant women in Rochester (NY). The levels were significantly higher in the present study. On the other hand, comparison of our data with a study by Sakamoto et al. [23] in Japanese pregnant, suggest lower concentrations of Pb (39.78 and 56.6 ng/g, respectively), Cd (19.92 and 68.6 ng/g, respectively) and Cu (0.94 and 3.91 μg/g, respectively) and higher levels of Zn (8.38 and 3.91 μg/g, respectively). Also our detected levels of Cu (0.94 and 4.87 μg/g, respectively) and Zn (8.38 and 62.6 μg/g, respectively) were significantly lower when comparing with Kantola et al. [24] while concentration of Cd (19.92 and 22.2 ng/g, respectively) was very similar in both studies. Slightly higher values of lead were detected in the present study in comparison with a cohort of pregnant women from Viena (39.78 and 26 ng/g, respectively). There is no threshold limit for placental lead levels and it is difficult to elucidate the potential impact of the Pb levels detected in this study on pregnancy outcome or cognitive development afterwards. But our results are below than levels than have shown previously adverse effects [22]. Cadmium exposure and accumulation in the body start at young age what deserves attention in order to limit as much as possible its serious health effects later in life [22]. Levels of Mn were similar in the present study in comparison with those detected by de Angelis et al. [5].

3.3. Inter-correlations among metals

Correlation analysis was performed in order to find out the possible interrelations among metal concentrations in placental tissue. The most important correlations (with a probability (P) of error level less than 0.05) were those with a Spearman coefficient > 0.5. To control multiple testing has been used post-hoc test as Bonferroni or Tamhane T tests. This analysis showed a significant positive correlation, close to 1, between Al and Ba (0.710; 95%CI 0.56; 0.82); Fe and B (0.940; 95% CI 0.90; 0.96); Ca and Mg (0.75; 95% CI 0.61; 0.84); Ca and Sr (0.730, 95% CI 0.58; 0.83); Pb and Sr (0.855, 95% CI 0.77; 0.91) whereas negative correlation only was found between Al and Na (-0.540, 95% CI -0.70; -0.34). These positive correlations may suggest that concentrations of these elements are influenced by similar underlying transport mechanisms (such as the transportation routes of Fe, Ca and Zn) and proteins (such as metallothioneins) [5].

3.4. Factors influencing the concentrations of metals in placenta samples

Bivariate associations between maternal characteristics, demographic and placental metal levels were only significant for Cd concentrations, which were higher in mothers smoking during pregnancy; In this case, placental Fe levels were significantly lower in mothers who were having Fe as dietary supplement than in those who were not having it. When Pearson's chi squared was applied to sets of categorical data, only maternal age range resulted significant related with previous premature labor. The increasing exposure to Cd due to smoking was previously demonstrating by Kantola et al. [24], whose detected higher concentration of this metal not only in placenta from smoker pregnant but also in whole blood and cord blood.

These factors that were shown to increase biological metal concentrations in the descriptive analysis, including demographic and lifestyle characteristics of the participants were then investigated for their potential contribution or influence on biological metals concentration using multiple linear regression. After a correlation study between the dependent and independent variables, only those whose significance was less than 0.25 have been incorporated into the multivariate model. The results for each metal are presented in Table 2 and briefly summarized below.

The variables studied represented a not significant contribution in placenta levels of Ca, Cd, Cr, Cu, K, Li, Mo, Na, Sr and V. Gestational age were the most important variable influencing Al, B, Ba, and Pb concentrations. Other factors influencing to Ba, Fe and Zn, Mg, were Fe supplementation, and maternal education. On the other hand, it was observed that the neonatal weight was influenced only for placental Ni concentration. Cigarette smoke contains nickel that once introduced into the respiratory tract may reach, cross and accumulate in human placentas. However, in the study of bivariate associations only Cd showed significant differences between smokers and non-smokers though represented a not significant contribution in the neonatal weight after the multiple linear regression study. In contrast, Ronco et al. [25] found that moderate smoking mothers deliver neonates with decreased birth weight and highly correlated to placental cadmium concentration. In a later study, Sabra et al. [26] didn't observe differences in the placental heavy metals (Cd, Pb and Zn) levels among three newborn groups (normal weight, fetal intrauterine growth restriction, and small for-gestational age).

We can conclude that the results of our study suggest that the main maternal determinant of detectable placenta Cd levels was smoking during pregnancy. Other maternal factors that may affect placenta metal levels are gestational age (Al, B, Ba, and Pb) or dietary iron supplemention.

These findings are important because it would mean that even low Ni exposure in both smokers and non-smokers pregnant can influence intrauterine growth. And probed how the soil contamination can influenced the concentration of heavy metals in placenta through diet.

Nonetheless, it has to be stressed that our results have to be interpreted with caution, because of the small study group and the low exposure levels, along with the lack of information on potential sources of exposure to these metals. The use of placenta samples obtained at delivery can be considered strength of this study since the concentration of some metals in placenta can indicate the extent of maternal exposure during gestation. This fact is due to when pregnant women are exposed to toxic metals; those metals can be transferred from the mother's blood to the developing fetus in part by binding to the placenta [27].

Research data for this article

Due to the sensitive nature of the questions asked in this study, survey respondents were assured raw data would remain confidential and would not be shared.

Data not available / The data that has been used is confidential.

Declarations of interest

None.

Conflict of interest

There is no conflict of interest.

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