Analysis of essential, toxic, rare earth, and noble elements in maternal and umbilical cord blood

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Abstract
Progressive industrialization in recent decades has contributed to the increase of metal levels in the environment, which has a dangerous impact on human health, primarily pregnant women. In this study, we aimed to compare levels of various elements in maternal and umbilical cord (UC) plasma samples collected from 125 healthy pregnant women, conduct correlation analysis among paired plasma samples, and compare our data with other populations worldwide. The study design included the following elements: essential (Mn, Co, Cu, Zn, Se, Mo), non-essential (Be, Al, Ni, As, Rb, Sr, Cd, Sb, Pb, U), rare earth (La, Pr, Ce, Nd, Sm, Eu, Gd, Dy, Ho, Er), and noble metals (Ru, Rh, Re, Pt). Levels of 30 elements were higher in maternal plasma than in UC plasma samples. However, no disparities at the statistically significant level were found for Be, Zn, Rb, Cd, Ce, and Ho. Correlation analysis among paired plasma samples revealed only positive/synergistic correlations of different strengths between most elements. Compared to other countries across the globe, our participants had considerably lower plasma levels of Zn and higher levels of Co, Ni, and As. This study provides not only a new and deeper comprehension, but also the first insight into the levels, correlation, distribution, and potential transplacental transfer of 30 elements.

Keywords Element · Maternal plasma · Umbilical cord plasma · Correlation analysis

Introduction
Human biomonitoring (HBM) has become a powerful tool in an algorithm for examining the impact of one or more natural or artificial environmental pollutants on health, particularly in pregnant women and children, as the most vulnerable population groups (Kot et al. 2019; Bocca et al. 2019). HBM studies aim to identify the type of pollutant and exposure route, find specific biomarkers, create normal intervals and establish a scientific database, assess health risks, assist in epidemiological, clinical, and other investigations, etc. (Černá et al. 2012). A new trend in HBM studies is the examination of solid tissues (e.g., placental, thyroid) instead of body fluids (e.g., serum/plasma, urine) and/or body products (e.g., feces), because each solid tissue has its blood supply and different accumulation capacity for both naturally occurring and anthropogenic origin pollutants (Stojsavljević and Rovčanin 2021). Among the well-identified harmful agents, some elements are recognized as hazardous to human health (Silver et al. 2018). Furthermore, as a result of growing industrialization, the level of these hazardous elements has risen notably in recent decades (Wang et al. 2019). Therefore, it is not unexpected that elements’ profiles differ among population groups across the globe and that it is necessary to monitor their levels in specific clinical samples (Serafim et al. 2012; Caserta et al. 2013).

The negative effects of elements are pronounced in the pre- and postnatal periods of life (Al-Saleh et al. 2013; Kozikowska et al. 2013). The prenatal period is particularly
critical because the fetus undergoes various morphological changes, which are directly dependent on environmental stimuli, even at low levels of exposure (Cerrillos et al. 2019). Due to exposure to specific elements, studies have reported permanent morphological alterations over the first 3 months of fetal development, whereas functional consequences were observed after the end of organogenesis for different degrees of exposure to the elements (Rudge et al. 2009; Al-Saleh et al. 2011). A good example is lead (Pb) since this heavy metal easily crosses the placental barrier and tends to accumulate in the fetus. Moreover, babies and children are subjected to Pb later in life, primarily through toys and dust, while their mothers and the population in general are primarily exposed to Pb via polluted air, contaminated drinking water and food, and so on (Reddy et al. 2014; Iwai-Shimada et al. 2019).

The first aim of this study was to compare levels of 30 elements in maternal and umbilical cord (UC) plasma samples. A further aim of this study was correlation analysis between the same elements in paired maternal and UC plasma samples. The last aim of this study was to compare the levels of investigated elements in maternal and UC plasma samples with other populations worldwide. In accordance with the aims, the following elements were enrolled in the study design: essential (Mn, Co, Cu, Zn, Se, Mo), non-essential (Be, Al, Ni, As, Rb, Sr, Cd, Sb, Pb, U), rare earth (La, Pr, Ce, Nd, Sm, Eu, Gd, Dy, Ho, Er), and noble elements (Ru, Rh, Re, Pt). These elements were selected due to a lack of knowledge about their levels and distribution, as well as their correlation, in maternal and UC plasma samples.

Materials and methods

Sample collection

One hundred and twenty-five pregnant women, aged 20–41 years, were included in this study. The course of pregnancy was regular, and each birth was in term. All participants were in excellent health, released from chronic diseases (previous history of malignancies, liver and renal dysfunctions, hypertension, type I or II diabetes, etc.), venous thrombosis, and complications during pregnancy (oligohydranmios, gestational diabetes, preeclampsia, and infection). They were also released from external factors, such as occupational exposure to heavy metals. Furthermore, ineligibility criteria were multi-fetal pregnancies, mothers who gave birth by elective or emergency cesarean section, prolonged labor, etc. Thus, only participants who had spontaneous, vaginal, and uncomplicated childbirth were recruited in this study. The data from participants were collected after the informed consent of each woman.

The investigation was approved by the Institutional Ethical Review Board (No: 05006-2021-1525).

At the beginning of the delivery phase, a sample of the mother’s venous blood was taken from the antecubital vein by venipuncture and collected into a lithium-heparin Vacutainer tube (BD Vacutainer Royal Green Cap, Becton Dickinson). A total of 5 mL of whole blood (arteriovenous) was drawn from the umbilical cord up to 5 min after birth, promptly after double tightening of the cord from the maternal umbilical end, but before the placental expulsion. Each sample of umbilical whole blood was collected into a Li-heparin Vacutainer tube from the same manufacturer. After centrifuging whole blood (3000 × g for 10 min), plasma samples from the mother and umbilical cord were separated from the blood cells. All samples were stored at −80 °C until analysis.

Analysis of elements

The procedure for element analysis was adapted from our previous study (Stojsavljević et al. 2018). Briefly, plasma samples were diluted 10-fold with an aqueous solution containing 0.05% nitric acid, 0.1% Triton X-100, and 3% n-butanol. All elements were quantified by inductively coupled plasma quadrupole mass spectrometry (ICP-Q-MS) in collisional (helium) mode and by adding an internal standard solution (71Ga, 115In, and 159Tb at concentrations of 10 μg/L), in equal amounts to each solution. Good linearity of the calibration curve ($R \geq 0.994$) was recorded for each element in the ranges from 1 to 250 μg/L (Cu, Zn, Se, Rb), 1–25 μg/L (Al, Mn, Co, Ni, As, Sr, Mo, Sb, Cd, Pb), or 0.1–25 μg/L (Be, Ru, Rh, La, Ce, Pr, Nd, Sm, Eu, Dy, Gd, Ho, Er, Re, Pt, U). All elements were successfully (100%) detected in the analyzed plasma samples. The accuracy of the method was tested with certified reference materials (CRMs) Serum Level-1 and Serum Level-2, supplied by Seronorm (Sero AS, Norway). The recoveries for the CRMs spanned from 80.4 to 118% (Table S1a, Suppl. material). Furthermore, the standard addition method was applied to evaluate the accuracy of the analytical technique used. Ten samples of maternal plasma and ten samples of UC plasma were spiked with a standard solution of each element (10 and 20 μg/L). The results are represented in Table S1b (Suppl. material). Based on the recoveries obtained by CRMs and the standard addition method, the following isotopes were chosen: $^9$Be, $^{27}$Al, $^{55}$Mn, $^{59}$Co, $^{60}$Ni, $^{63}$Cu, $^{67}$Zn, $^{75}$As, $^{78/82}$Se, $^{87}$Rb, $^{88}$Sr, $^{98}$Mo, $^{101}$Ru, $^{103}$Rh, $^{111}$Cd, $^{121}$Sb, $^{139}$La, $^{141}$Pr, $^{142}$Ce, $^{146}$Nd, $^{152}$Sm, $^{153}$Eu, $^{158}$Gd, $^{162}$Dy, $^{165}$Ho, $^{167}$Er, $^{185}$Re, $^{196}$Pt, $^{208}$Pb, and $^{238}$U.
Data analysis

The results were processed using SPSS v.25 statistical software package (SPSS Inc., Chicago, Ill.), while all figures were drawn using GraphPad Prism v.5.0 (CA, USA). The Kolmogorov-Smirnov test was used to check the normality of the data. Differences between elemental levels were analyzed using Chi-square test, Kruskal-Wallis one-way analysis of variance, and Mann-Whitney U test. The Spearman’s rho (ρ) correlation test was used to examine the correlation analysis between maternal and UC plasma for each element. In all tests used, \( P < 0.05 \) was considered statistically significant.

Results

The most relevant parameters for pregnant women and their newborns are shown in Table 1. It is evident that the enrolled group of participants was notably homogeneous in terms of maternal age and pregnancy duration. Correlation analysis was not conducted for these data since none of the pregnant women smoked or used alcohol and/or drugs. Moreover, none of the participants were professionally exposed to heavy metals. All pregnancies were singleton with a gestational age of 38–42 weeks, while Apgar scores were ≥ 9 in the first minute of postnatal life. Anthropometric parameters of the newborn (weight and height) were within the reference ranges, additionally implying a normal course of pregnancy.

Fig. 1 shows the map of Serbia. The shaded fields represent Belgrade and two regions (Šumadija and Podunavlje) from where the samples of participants were acquired. The Chi-square test did not reveal statistically significant differences in the elemental levels in maternal and UC plasma samples between women residing in different regions. This finding could be explained by a similar diet of the examined pregnant women.

The distribution of analyzed elements in the maternal and umbilical cord (UC) plasma samples, based on their values of mean and standard deviation (SD), is given in Figs. 2 and 3. Copper (Cu) was the most dominant element in maternal plasma samples, while it was the second most abundant in UC plasma samples; in these, the first place belonged to zinc (Zn). Holmium (Ho) was the element with the lowest detected levels in both maternal and UC plasma samples. Data from Fig. 2 are further specified in Table 2, together with the \( P \) values obtained by the Mann-Whitney \( U \) test. Maternal plasma samples had higher levels of each analyzed element compared to UC plasma samples; however, no statistically significant differences were found for beryllium (Be), Zn, rubidium (Rb), cadmium (Cd), cerium (Ce), and Ho. Also, comparing maternal and UC plasma samples, the levels of Rb and Ce were very similar, while maternal/UC levels for other elements were more disparate (Table 2). Table 3 shows the correlation analysis between the same elements in maternal and UC plasma samples. Surprisingly, only positive correlations of varying strength were discovered among the elements. However, comparing maternal and UC plasma samples, levels of aluminum (Al), nickel (Ni), arsenic (As), selenium (Se), strontium (Sr), and platinum (Pt) were not statistically significantly correlated between the two plasma types.

Discussion

Our results showed that the levels of all analyzed elements were higher in maternal than in UC plasma samples. However, not all studied elements had statistically significantly different levels between paired maternal and UC plasma samples. Thus, no disparities were found for Be, Zn, Rb, Cd, Ce, and Ho levels in the two plasma types (\( P > 0.05 \)). Among these elements, the levels of Zn and Cd have been previously reported while the biochemical functions of Be, Rb, Ce, and Ho remain insufficiently explored. Our data could imply that the fetus withdraws essential Zn from the mother’s bloodstream, which could be a reason for the strong positive/synergistic correlation obtained between the maternal and UC plasma samples for this metal (\( \rho = 0.73 \)). Moreover, this finding should also be interpreted taking into account the previously reported Zn deficiency in our adult population (Jagodić et al. 2021). Therefore, the notably low Zn levels in both our types of plasma samples indicate

Table 1 The most representative parameters for women and their newborns enrolled in the research

| Parameter                        | Value (range) |
|----------------------------------|---------------|
| Mother age (years)               | 28.2 ± 4.31 (20–41)a |
| Gestation length (weeks)         | 39.0 ± 0.75 (38–42)a |
| Number of previous pregnancies   | None (n = 80)b       |
| Residence (capital/other)        | 111/14b         |
| Cigarette smoker (yes/no)        | 0/125b          |
| Alcohol consumer (yes/no)        | 0/125b          |
| Drug addiction history (yes/no)  | 0/125b          |
| Professional exposure to metals  | 0/125b          |
| (yes/no)                         |                |
| In vitro fertilization (yes/no)  | 0/125b          |
| Newborn sex (male/female)        | 66/59b          |
| Newborn height (cm)              | 50.1 ± 1.63 (47–57)a |
| Newborn weight (kg)              | 3.39 ± 0.41 (2.62–4.19)a |

\( ^{a} \) Data are presented as mean ± standard deviation

\( ^{b} \) Data are presented as frequencies
Fig. 1 The shaded fields on the map of Serbia represent the capital (Belgrade), Šumadija, and Podunavlje, from where samples of participants were acquired.

Fig. 2 Distribution of 30 analyzed elements in maternal plasma samples presented as mean ± standard deviation (μg/L).
the need for oral Zn-salt supplementation and/or increased intake of Zn-rich foods.

The placenta has been indicated to function as a barrier against Cd toxicity (Al-Saleh et al. 2013). Although inconclusive reports were identified among studies, new research has shown that the placenta has the ability to accumulate Cd and increase the expression of metallothioneins (MTs), small proteins that efficiently bind Cd$^{2+}$ and reduce its toxicity (Somsuan et al. 2019; Mazurek et al. 2020). However, MTs also bind Zn$^{2+}$ ions, which could explain a lack of Zn if an increased Cd level is present (Iwai-Shimada et al. 2019). Sakamoto et al. (2018) reported statistically higher levels of Cd in maternal plasma samples compared to UC ones. Our data were in agreement with their study, although we did not find a statistically significant value ($P = 0.075$) between maternal (0.47 ± 0.31 μg/L) and UC plasma samples (0.31 ± 0.15 μg/L).

Other analyzed elements occurred at significantly different levels in maternal and UC blood plasma samples (Table 2). Among them, and to the best of our knowledge, literature data are available for Mn, Co, Ni, Cu, As, Se, Mo, and Pb. Mn is an important antioxidant nutrient and essential trace metal for embryogenesis, myelin development, skeletal formation, etc. (Silver et al. 2018), while elevated Mn levels could be related to complications in fetal nervous system development, gestational hypertension, attenuated effects on birth weight, etc. (Zhou et al. 2019). Our Mn levels in maternal plasma samples were slightly higher than reported data (Burtis et al. 2012). Also, UC plasma samples (1.61 ± 0.81 μg/L) had slightly lower Mn levels compared to those reported from several Asian countries, including Japan (4.54 ± 1.21 μg/L) (Osada et al. 2002), Anhui Province, China (5.44 μg/L) (Liang et al. 2019), and Zhejiang province, China (4.20 μg/L) (Silver et al. 2018), but were in good agreement with Mn in UC plasma samples collected from Valencia, Spain (2.92 μg/L) (Bermúdez et al. 2015).

The notably high Co levels recorded in both types of plasma samples can be clarified by the use of supplements containing vitamin B12, since 85% of the human body’s Co content is in this form (Bocca et al. 2019). As a result, no comparison with research from other nations has been conducted, considering pregnant women in Serbia frequently take B12 supplements from different manufacturers in varying doses.

The considerably high Ni levels in maternal and UC plasma samples agreed with our previously reported high Ni levels in placental samples from the same participants (Stojsavljević et al. 2021). Since Ni-contaminated food and drinking water are the main sources of this metal, along with Ni-containing products (cosmetics, jewelry, etc.) (Bocca et al. 2020), it is difficult to ascertain the exact routes of Ni exposure. However, notably high Ni levels deserve further analysis, as studies have shown an association between high Ni levels and some disturbances in anthropometric parameters, gestational hypertension, and impaired neurodevelopment (Kot et al. 2019).

Cu is necessary for proper fetus growth and many life-supporting biochemical pathways. Our data for Cu in maternal plasma samples (2127 ± 523 μg/L) were consistent with previously published findings (Butler Walker et al. 2006a, b; Bermúdez et al. 2015), as estrogen is known to increase Cu levels through enhanced ceruloplasmin expression. Also, the mean Cu level in UC plasma samples (276 ± 114 μg/L) was consistent with other studies worldwide, including 54 participants from Valencia, Spain (248 μg/L) (Bermúdez et al. 2015), 357 participants from Zhejiang Province, China (243 μg/L) (Silver et al. 2018), and 2382 participants from Anhui Province, China (300 μg/L) (Liang et al. 2019).

Curiously, compared to other data worldwide, we found notably higher As levels in maternal and UC plasma samples (up to 10-fold higher). For example, Liang et al. (2019) reported 1.87 μg/L in UC plasma samples, while McKeating et al. (2020) recorded 0.90 ± 1.83 μg/L in the same sample type. However, Bermúdez et al. (2015) reported 19.9 μg/L in UC plasma, similar to our mean UC plasma level. Since our participants had a normal diet, typical for pregnancy, high As levels should be examined further by applying speciation analysis, since our population is not known for consuming significant amounts of fish or seafood, which are the most dominant sources of organic (harmless) forms of As. In addition to Ni, the findings for As are worrisome, since As easily crosses the placenta and increases the likelihood of preterm birth, fetal loss, and neonatal mortality, while it reduces birth weight and children’s thymus size, especially in countries with As-contaminated drinking water, such as Bangladesh and India (Cardenas et al. 2015; Ahmed et al. 2011).
Table 2 Results for LOD, range (min-max), and mean and standard deviation (SD) for the analyzed elements in maternal and umbilical cord (UC) plasma samples (μg/L). Statistically significant differences between the two plasma types are given in bold.

| Element | Sample     | LOD    | Range (min-max) | Mean ± SD | P value* |
|---------|------------|--------|-----------------|-----------|----------|
| Be      | Maternal plasma | 0.0003 | 0.03–0.69       | 0.21±0.14 | 0.056    |
|         | UC plasma   |        |                 |           |          |
| Al      | Maternal plasma | 0.012  | 1.30–97.6       | 26.2±16.0 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Mn      | Maternal plasma | 0.04   | 1.72–64.1       | 4.51±1.13 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Co      | Maternal plasma | 0.03   | 5.40–34.6       | 8.97±1.23 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Ni      | Maternal plasma | 0.50   | 75.1–169        | 125±18.4  | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Cu      | Maternal plasma | 5.4    | 548–3446        | 2127±523  | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Zn      | Maternal plasma | 5.9    | 180–1421        | 484±145  | 0.077   |
|         | UC plasma   |        |                 |           |          |
| As      | Maternal plasma | 0.03   | 16.7–61.2       | 34.8±7.38 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Se      | Maternal plasma | 1.1    | 54.8–248        | 135±30.9  | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Rb      | Maternal plasma | 2.4    | 63.4–244        | 146±36.7  | 0.063   |
|         | UC plasma   |        |                 |           |          |
| Sr      | Maternal plasma | 0.37   | 15.3–68.4       | 31.3±10.4 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Mo      | Maternal plasma | 0.004  | 1.75–297        | 4.76±1.66 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Ru      | Maternal plasma | 0.006  | 0.11–0.83       | 0.42±0.15 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Rh      | Maternal plasma | 0.001  | 0.12–0.68       | 0.41±0.10 | <0.01   |
|         | UC plasma   |        |                 |           |          |
| Cd      | Maternal plasma | 0.002  | 0.04–2.61       | 0.47±0.31 | 0.075   |
|         | UC plasma   |        |                 |           |          |

*P values were determined by the Mann-Whitney U test at a significant level below 0.05
Table 3  Correlation analysis between the same elements in maternal and umbilical cord (UC) plasma samples. Statistically significant correlations obtained using Spearman’s ρ are given in bold.

| Element in maternal plasma | Element in UC plasma | P     | Element in maternal plasma | Element in UC plasma | ρ     |
|----------------------------|---------------------|-------|----------------------------|---------------------|-------|
| Be                         | Be                  | 0.55  | Sb                         | Sb                  | 0.76  |
| Al                         | Al                  | 0.24  | La                         | La                  | 0.55  |
| Mn                         | Mn                  | 0.65  | Pr                         | Pr                  | 0.57  |
| Co                         | Co                  | 0.51  | Ce                         | Ce                  | 0.55  |
| Ni                         | Ni                  | 0.32  | Nd                         | Nd                  | 0.51  |
| Cu                         | Cu                  | 0.70  | Sm                         | Sm                  | 0.54  |
| Zn                         | Zn                  | 0.73  | Eu                         | Eu                  | 0.56  |
| As                         | As                  | 0.26  | Gd                         | Gd                  | 0.52  |
| Se                         | Se                  | 0.28  | Dy                         | Dy                  | 0.54  |
| Rb                         | Rb                  | 0.49  | Ho                         | Ho                  | 0.53  |
| Sr                         | Sr                  | 0.15  | Er                         | Er                  | 0.55  |
| Mo                         | Mo                  | 0.64  | Re                         | Re                  | 0.50  |
| Ru                         | Ru                  | 0.57  | Pt                         | Pt                  | 0.41  |
| Rh                         | Rh                  | 0.54  | Pb                         | Pb                  | 0.73  |
| Cd                         | Cd                  | 0.86  | U                          | U                   | 0.74  |

Limitations

This study is limited to the number of samples according to age, lifestyle, place of residence, etc. Furthermore, mercury was not reported due to strong memory effects during measurements on the ICP-MS device.

Conclusion

In summary, we assessed exposure to essential, non-essential, rare earth, and noble elements in paired maternal and umbilical cord plasma samples. Levels of all elements were higher in maternal plasma than in UC plasma; however, no disparities at a statistically significant level were found for Be, Zn, Rb, Cd, Ce, and Ho. Correlation analysis among paired plasma samples revealed only positive/synergistic correlations of different strengths between most elements. Compared to other countries worldwide, our participants had notably higher levels of Co, Ni, and As and lower levels of Zn in their plasma. This research brings not only a new and deeper comprehension, but also the first insight into the levels, distribution, correlation analysis, and potential transplacental transfer of 30 elements. The results presented in this study can be utilized as a database for risk assessment of the pregnancy outcomes and as a starting point for further toxicological, epidemiological, clinical, and other peer-reviewed studies.

Availability of data and material  Data and material are available from the corresponding author on reasonable request.

Author contribution  A.S. designed the study, analyzed the elements in samples, conducted statistical analysis, and wrote the first and last versions of the manuscript; M.R. collected clinical samples; N.Z., Ž.M., A.J., M.P., and D.M. participated in reviewing and editing. All authors read the paper and gave final approval for publication.

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Declarations

Ethics approval  The investigation was approved by the Institutional Ethical Review Board (No: 05006-2021-1525).

Consent to participate  All women voluntarily participated in this study, and written informed consent from all study participants was obtained according to the ethical standards defined by the Declaration of Helsinki.
Consent for publication Not applicable.

Conflict of interest The authors declare no competing interests.

References

Al-Saleh I, Shinwari N, Mashhour A, Mohamed Gel D, Rabah A (2011) Heavy metals (lead, cadmium and mercury) in maternal, cord blood and placenta of healthy women. Int J Hyg Environ Health 214:79–101. https://doi.org/10.1016/j.ijeh.2010.10.001

Al-Saleh I, Shinwari N, Mashhour A, Rabah A (2013) Birth outcome measures and maternal exposure to heavy metals (lead, cadmium and mercury) in Saudi Arabian population. Int J Hyg Environ Health 217:205–218. https://doi.org/10.1016/j.ijeh.2013.04.009

Bermtüdez L, García-Vicent C, López J, Torró MI, Lurbe E (2015) Assessment of ten trace elements in umbilical cord blood and maternal blood: association with birth weight. J Transl Med 13:291. https://doi.org/10.1186/s12967-015-0654-2

Bocca B, Ruggieri F, Pino A, Rogiva J, Calamandrei G, Martínez MÁ, Domingo JL, Alimonti A, Schuhmacher M (2019) Human biomonitoring to evaluate exposure to toxic and essential trace elements during pregnancy. Part A: concentrations in maternal blood, urine and cord blood. Environ Res 177:108599. https://doi.org/10.1016/j.envres.2019.109108

Bocca B, Ruggieri F, Pino A, Rogiva J, Calamandrei G, Mirabella F, Martínez MÁ, Domingo JL, Alimonti A, Schuhmacher M (2020) Human biomonitoring to evaluate exposure to toxic and essential trace elements during pregnancy. Part B: Predictors of exposure. Environ Res 182:109108. https://doi.org/10.1016/j.envres.2019.109108

Butter CA, Ashwood ER, Bruns DE, Tietz NW (2012) Textbook of clinical chemistry and molecular diagnostics, 5th ed., Elsevier. ISBN: 978-1-4160-6164-9

Butler Walker J, Houseman J, Seddon L, McMullen E, Tofflemire K, Mills C, Corriveau A, Weber JP, LeBlanc A, Walker M, Donaldson SG, Van Oostdam J (2006a) Maternal and umbilical cord blood levels of mercury, lead, cadmium, and essential trace elements in Arctic Canada. Environ Res 100:295–318. https://doi.org/10.1016/j.envres.2005.05.006

Butler Walker J, Houseman J, Seddon L, McMullen E, Tofflemire K, Mills C, Corriveau A, Weber JP, LeBlanc A, Walker M, Donaldson SG, Van Oostdam J (2006b) Maternal and umbilical cord blood levels of mercury, lead, cadmium, and essential trace elements in Arctic Canada. Environ Res 100:295–318. https://doi.org/10.1016/j.envres.2005.05.006

Cardenas A, Koestler DC, Houseman EA, Jackson BP, Kile ML, Karagas MR, Maris JT (2015) Differential DNA methylation in umbilical cord blood of infants exposed to mercury and arsenic in utero. Epigenetics 10:508–515. https://doi.org/10.1080/15592294.2015.1046026

Caserta D, Graziano A, Lo Monte G, Bordi G, Moscarini M (2013) Heavy metals and placental fetal-maternal barrier: a mini-review on the major concerns. Eur Rev Med Pharmacol Sci 17:2198–2206

Cerná M, Krsková A, Cechanová M, Spěváčková V (2012) Human biomonitoring in the Czech Republic: an overview. Int J Hyg Environ Health 215:109–119. https://doi.org/10.1016/j.ijeh.2011.09.007

Cerrillos L, Fernandez R, Machado MJ, Morillas I, Dahiari B, Paz S, Gonzalez-Weller D, Gutierrez A, Rubio C, Hardisson A, Moreno I, Fernandez-Palacin A (2019) Placental levels of metals and associated factors in urban and sub-urban areas of Seville (Spain). J Trace Elem Med Biol 54:21–26. https://doi.org/10.1016/j.jtemb.2019.03.006

Dursun A, Yurdakok K, Yalcin SS, Tekinalp G, Aykut O, Orhan G, Morgil GK (2016) Maternal risk factors associated with lead, mercury and cadmium levels in umbilical cord blood, breast milk and newborn hair. J Matern Fetal Neonatal Med 29:954–961. https://doi.org/10.3109/14767058.2015.1026255

Iwai-Shimada M, Kameo S, Nakai K, Yaginuma-Sakurai K, Tatsuta N, Kurokawa N, Nakayama SF, Satoh H (2019) Exposure profile of mercury, lead, cadmium, arsenic, antimony, copper, selenium and zinc in maternal, cord blood and placenta: the Tohoku study of child development in Japan. Environ Health Prev Med 17:24–35. https://doi.org/10.1186/s12967-019-0783-y

Jagodić I, Rovčanin B, Borković-Mitić S, Lj V, Avdin V, Manoilović D, Stojašević A (2021) Possible zinc deficiency in the Serbian population: examination of body fluids, whole blood and solid tissues. Environ Sci Pollut Res Int 24:1–8. https://doi.org/10.1007/s11356-021-14013-2

Kot K, Kosik-Bogacka D, Lanocha-Arendarczyk N, Malinowski W, Szymański S, Mularczyk M, Tomńska N, Roter I (2019) Interactions between 14 elements in the human placenta, fetal membrane and umbilical cord. Int J Environ Res Public Health 16:1615. https://doi.org/10.3390/ijerph16091615

Kozikowska I, Binkowski LJ, Szczepanska K, Sławska H, Miszczuk K, Sliwińska M, Laciak T, Stawarz R (2013) Mercury concentrations in human placenta, umbilical cord, cord blood and amniotic fluid and their relations with body parameters of newborns. Environ Pollut 182:256–262. https://doi.org/10.1016/j.envpol.2013.07.030

Liang C, Li Z, Xia X, Wang Q, Tao R, Tao Y, Xiang H, Tong S, Tao F (2017) Determine multiple elements simultaneously in the sera of umbilical cord blood samples—a very simple method. Biol Trace Elem Res 177:1–8. https://doi.org/10.1007/s12011-016-0853-6

Liang CM, Wu XY, Huang K, Yan SQ, Li ZJ, Xia X, Pan WJ, Sheng J, Tao YR, Xiang HY, Hao JH, Wang QN, Tao FB, Tong SL (2019) Trace element profiles in pregnant women’s sera and umbilical cord sera and influencing factors: repeated measurements. Chemosphere 218:869–878. https://doi.org/10.1016/j.chemosphere.2018.11.115

Mazurek D, Lozka K, Bronkowska M (2020) The concentration of selected elements in the placenta according to selected sociodemographic factors and their effect on birth mass and birth length of newborns. J Trace Elem Med Biol 58. https://doi.org/10.1016/j.jtemb.2019.126425

McKeating DR, Fisher JJ, Zhang P, Bennett WW, Perkins AV (2020) Elemental metabolomics in human cord blood: method validation and trace element quantification. J Trace Elem Med Biol 59:126419. https://doi.org/10.1016/j.jtemb.2019.126419

Osada H, Watanabe Y, Nishimura Y, Yuka M, Seki K, Sekiya S (2002) Profile of trace element concentrations in the feto-placental unit in relation to fetal growth. Acta Obstet Gynecol Scand 81:931–937. https://doi.org/10.1034/j.1600-0412.2002.811006.x

Parizi MG, Sedaghat Z, Mazloomi M et al (2021) (2021) Serum level of lead and cadmium is linked to facial cosmetics use among Iranian young women. Environ Sci Pollut Res 28:1393–13918. https://doi.org/10.1007/s11356-020-11618-x

Reddy YS, Aparna Y, Ramalaksmi BA, Kumar BD (2014) Lead and trace element levels in placenta, maternal and cord blood: a cross-sectional pilot study. J Obstet Gynaecol Res 40:2184–2190. https://doi.org/10.1111/jog.12469

Rudge CV, Röllin HB, Nogueira CM, Thomassen Y, Rudge MC, Odland JØ (2009) The placenta as a barrier for toxic and essential elements in paired maternal and cord blood samples of South African delivering women. J Environ Monit 11:1322–1330. https://doi.org/10.1039/b903805a

Sakamoto M, Chan HM, Domingo JL, Koriyama C, Murata K (2018) Placental transfer and levels of mercury, selenium, vitamin E, and
docsodhexaenoic acid in maternal and umbilical cord blood. Environ Int 111:309–315. https://doi.org/10.1016/j.envint.2017.11.001
Serafim A, Company R, Lopes B, Rosa J, Cavaco A, Castela G, Castela E, Olea N, Bebianno MJ (2012) Assessment of essential and non-essential metals and different metal exposure biomarkers in the human placenta in a population from the south of Portugal. J Toxicol Environ Health A 75:867–877. https://doi.org/10.1080/15287394.2012.690704
Silver MK, Arain AL, Shao J, Chen M, Xia Y, Lozoff B, Meeker JD (2018) Distribution and predictors of 20 toxic and essential metals in the umbilical cord blood of Chinese newborns. Chemosphere 210:1167–1175. https://doi.org/10.1016/j.chemosphere.2018.07.124
Somsuan K, Phuapittayalert L, Srithongchai Y et al (2019) Increased DMT-1 expression in placentas of women living in high-Cd-contaminated areas of Thailand. Environ Sci Pollut Res 26:141–151. https://doi.org/10.1007/s11356-018-3598-2
Stojavljević A, Rovčanin M, Rovčanin B, Miković Ž, Jeremić A, Perović M, Manojlović D (2021) Human biomonitoring of essential, nonessential, rare earth, and noble elements in placental tissues. Chemosphere 285:131518. https://doi.org/10.1016/j.chemosphere.2021.131518
Stojavljević A, Trifković J, Rasić-Milutinović Z, Jovanović D, Bogdanović G, Mutić J, Manojlović D (2018) Determination of toxic and essential trace elements in serum of healthy and hypothyroid respondents by ICP-MS: a chemometric approach for discrimination of hypothyroidism. J Trace Elem Med Biol 48:134–140. https://doi.org/10.1016/j.jtemb.2018.03.020
Stojavljević A, Rovčanin B (2021) Impact of essential and toxic trace metals on thyroid health and cancer: a review. Expo Health. https://doi.org/10.1007/s12403-021-00406-8
Wang X, Qi L, Peng Y et al (2019) Urinary concentrations of environmental metals and associating factors in pregnant women. Environ Sci Pollut Res 26:13464–13475. https://doi.org/10.1007/s11356-019-04731-z
Zhou C, Zhang R, Cai X, Xiao R, Yu H (2019) Trace elements profiles of maternal blood, umbilical cord blood, and placenta in Beijing, China. J Matern Fetal Neonatal Med 32:1755–1761. https://doi.org/10.1080/14767058.2017.1416602

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