Determination of Toxic Metals Burden and Related Risk Factors in Pregnant Women: A Biological Monitoring in Sabzevar, Iran

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Abstract

Background

Nowadays, the adverse effect of toxic metals on humans is well-known especially in the fetal period such as preventing cognitive development and congenital abnormalities of the central nervous system.

Methods

This study aims to evaluate the toxic metals burden in mothers and newborns in Sabzevar. One hundred eighty samples including placental blood and umbilical cord blood were taken from ninety mothers referred to Shahidan Mobini Hospital for delivery. The samples were analyzed using inductively-coupled plasma optical emission spectrometry (ICP OES).

Results

The results of this study revealed that 21.52%, 26.19%, and 60.71% of maternal blood samples (placental blood) and 16.47%, 56.47% and 20% of umbilical cord blood samples were higher than the US centers for disease control (CDC) recommended levels for Pb, Cd and As respectively. According to the multiple linear regression analysis, the Pb ($p=0.054$), As ($p<0.001$), and Se ($p<0.001$) levels had an association with the mother's living area. Also, there is significant association between Se (0.021) and age of the mother.

Conclusion

However, the Se values in its optimum concentrations in the blood (60-140 $\mu\text{g/L}$) can decrease the adverse effects of toxic metals, 72.5% of the pregnant women had Se values below the 60 $\mu\text{g/L}$ and only 6% of pregnant women had Se levels higher than 140 $\mu\text{g/L}$. We concluded that the mothers inhabiting in the rural areas need more Se sources in their diets.

1. Introduction

Many health problems directly caused by environmental pollutions and toxic metals including mercury (Hg), cadmium (Cd), lead (Pb), and arsenic (As) (as a metalloid) that increasingly continued because of fast industrial development. These toxic metals can easily diffuse everywhere and accumulate in living organism's bodies through the food chain (Sakamoto et al. 2010; Hinwood et al. 2013). The toxic metals can enter the human body via contaminated water, food, and soil which cause several health problems (Ghasemi et al. 2019; Mohammadnia et al. 2019). Numerous investigations have shown that toxic metals have significant adverse effects on the health of children and adults (Satarug et al. 2009). Investigation of the effects of these pollutants on public health especially on children's growth and brain development is very important. The fetal stage is considered as the most sensitive developing stage because of the high rates of cell division and differentiation (Al-Saleh et al. 2011). These contaminations are also a threat to the fetus.

Many studies have confirmed the transfer of toxic metals and toxic compounds such as methyl mercury (MeHg), Cd, Pb, As and selenium (Se) from mother to fetus via placenta (Butler Walker et al. 2006; Sakamoto et al. 2010, 2012). Among these, Cd is a great danger to the fetus because of its adverse effects (García-Esquinas et al. 2013). The placenta is like a barrier that protects the fetus from toxic metals by releasing the metallothionein (McAleer and Tuan 2001). Even in the low concentrations, Cd can result in low birth weight (Li et al. 2019), premature delivery (Nishijo et al. 2002), and change of thyroid hormone levels in newborns (Iijima et al. 2007). It should be noted that Cd is highly absorbed into the human body by smoking (Thompson and Bannigan 2008). For non-smokers, contaminated water and occupational exposure are the main sources of Cd intake (Nishijo et al. 2004; Oskarsson et al. 2004). On the other hand, long exposures to Pb can cause miscarriage (Borja-Aburto et al. 1999), congenital malformations (Linn and Schoenbaum 1984), spontaneous abortion, low

birth length (Hernandez-Avila et al. 2002), high blood pressure in pregnancy (Kennedy et al. 2012) and impaired neurodevelopment (Bellinger et al. 1986). Moreover, occupational exposure to Hg has been reported to cause pregnancy-induced hypertension (Pan et al. 2007), decreased birth weight (Ramon et al. 2009), birth malformations (Jin et al. 2013), developmental delays, and memory loss (Jedrychowski et al. 2006).

There is a direct correlation between the amount of As in water and food and the incidence of diseases in adults and defects in fetuses (Walvekar et al. 2007) as transfers across the placental barrier and causes disorders in the growth trend. In this regard, delayed neonatal growth (Faita et al. 2013), increased mortality and neurological tube defects have been reported (Jin et al. 2006). Se (as a metalloid) is a rare element that is essential for the normal growth and development of organs. In pregnant women, Se levels in the blood and plasma usually decrease during pregnancy (Zachara et al. 2001). The presence of Se in the mother's blood prevents many of the toxins from entering the fetus's body (Magos et al. 1980). Considering the harmful effects of Cd, Hg, Pb and As on pregnant women and fetuses, and relatively high exposure to these toxic metals in the city of Sabzevar, it is necessary to monitor the health of mothers and newborns.

The present study for the first time in Sabzevar aimed to investigate the toxic metals in mothers and fetuses, risk factor determination, and also the association with some variables such as the mother's age, newborn's sex, living area, abortion and number of the filled teeth.

The data of this work can be helpful for other researchers and also cover some gaps existing in some databases facing insufficient data from Iranian society about maternal and fetal toxic metals burden.

2. Materials And Methods

2.1. Study site, questionnaire, sampling and data gathering

As figure 1 shows, Sabzevar city is located in Khorasan Razavi province in the northeast of Iran with a population of 500,000 (including 180 satellite rural areas). It is estimated that approximately 13,000 babies are born annually in Shahidan Mobini Hospital in Sabzevar city. In this study, 90 pregnant mothers were selected (according to statistical estimation) among all pregnant women referred to the hospital during the years 2016 to 2018 who had the required criteria for the study. Of these, about 50% were living in rural areas and the remainder were from Sabzevar city as urban livings.

To evaluate the factors affecting the concentration of toxic metals such as cadmium, mercury, arsenic (as a metalloid), and lead in the maternal and newborns blood, a questionnaire was designed in which eligible pregnant women should answer specified questions with satisfaction and complete knowledge of the study process.

The questions were about age, abortion, number of pregnancies, newborn's gender, living area, filled teeth, and specific disease record. The women who had chronic illnesses such as diabetes, hypertension, kidney disease, alcohol drinking, and multiple births, were excluded from the sampling process.

The samples were included placental blood and umbilical cord blood taken immediately after delivery. The sampling was done under ethical approval from the Ethics Committee of Sabzevar University of Medical Sciences (Code: IR.MEDSAB.REC.1395.67) and all participants signed the informed consent before including to the study.

2.2. Sample analyzing

Due to the least suffering mothers in the sampling process, the placental blood samples (representing the maternal blood) were taken from the maternal section of the placenta that contains endometrial arteries. As well as the blood samples for newborns, were taken from the umbilical cord representing the fetal blood. Ten-milliliter of each blood samples were transferred to heparin-coated polyethylene tube and first centrifuged (Hettich, Germany) at 3000 rpm for 10 minutes while red blood cells were separated, and the sample was dried in an oven (ATRA, Iran) at 65 °C for 48 h and a homogenized powder was prepared for acid digestion.

The digestion process was done using a Teflon vessel containing 5 ml concentrated HNO₃ and 0.2 gr powdered sample for one hour at room temperature. After that, the Teflon vessels were placed in a stepwise heating microwave digester (ETHOS UP, Italy) for one hour at 200 °C. After cooling down to room temperature, the clear supernatant was separated and diluted to 50 ml with deionized water and analyzed using inductively-coupled plasma optical emission spectrometry (ICP OES, LIBERTY-RL, Series II, Australia).

2.3. Statistical analyses

Testing for normality of data performed using the Shapiro-Wilk test. Toxic metals were estimated according to the independent variables as median with 75th and 25th percentiles. Correlation between toxic metals in the placental blood and umbilical cord blood demonstrated by Spearman's rank correlations. For examining the association between toxic metals and related determinants, univariate and multiple linear regression analyses were used.

All independent variables that had a significant association with the level of 0.2 were included in the multiple models for adjusting the potential confounders. The results were evaluated with a confidence level of 95% (P-value less than or equal to 0.05). Stata software (Version 12, Stata Corp, College Station, Texas, USA) was applied to analyze the data obtained from the questionnaires.

3. Results And Discussion

3.1. Descriptive statistics

In the present work, the age of pregnant women was in the range of 15-45 years with an average of 27.11 ± 6 years (Mean $\pm$ SD). Descriptive statistics and the median values (Q1-Q3) for Cd, As, Pb, and Se in the blood of placenta and umbilical cord samples are shown in Table 1.

Table 1

Descriptive statistics for values of toxic metals (µg/L) in the placental blood and umbilical cord blood samples according to related variables

Independent variables		As		Se		Cd		Pb	
		Placenta blood	Umbilical cord blood	Placenta blood	Umbilical cord blood	Placenta blood	Umbilical cord blood	Placenta blood	Umbilical cord blood
		Median	Median	Median	Median	Median	Median	Median	Median
		(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)
Living area	Urban	0.95 (0.66-1.42)	0.80 (0.47-1.61)	19.10 (10.64-34.41)	14.92 (8.46-30.32)	0.095 (0.0-0.57)	0.095 (0.0-0.19)	23.66 (4.23-58.79)	23.05 (2.94-57.50)
	Rural	5.27 (0.58-10.45)	3.18 (0.47-5.41)	95.53 (19.58-113.11)	68.15 (14.92-142)	0.19 (0.095-0.28)	0.095 (0.0-0.19)	27.75 (19.011-35.26)	27.56 (12.26-33.46)
Sex	Male	1.37 (0.66-8.46)	1.04 (0.28-4.18)	26.61 (11.31-98.85)	19.15 (9.55-121.38)	0.19 (0.09-0.33)	0.095 (0.0-0.19)	28.42 (16.53-41.44)	26.42 (13.02-43.29)
	Female	1.04 (0.66-2.94)	1.66 (0.66-3.61)	29.56 (17.20-44.77)	21.95 (11.69-46.19)	0.095 (0.0-0.32)	0.095 (0.0-0.19)	19.29 (4.75-39.44)	25 (3.56-43.29)
Filled teeth	0	1.42 (0.66-8.46)	1.52 (0.47-4.65)	32.41 (17.01-100.66)	30.89 (10.64-110.55)	0.19 (0.095-0.47)	0.095 (0.0-0.19)	27.94 (10.26-41.44)	25.38 (12.26-36.69)
	1≤	0.95 (0.66-1.99)	1.09 (0.28-2.89)	19.58 (10.64-42.20)	15.96 (10.59-3.12)	0.095 (0.0-0.28)	0.095 (0.0-0.19)	19.86 (4.08-43.91)	27.89 (2.66-53.89)
Mother's age (Years)	<25	1.23 (0.66-2.94)	1.04 (0.47-3.89)	24.80 (17.01-43.48)	18.67 (11.69-34.31)	0.095 (0.0-0.28)	0.095 (0.0-0.19)	20.81 (7.31-41.44)	19.58 (1.18-43.72)
	25≤	1.28 (0.66-8.84)	1.71 (0.38-3.99)	38.30 (10.97-103.56)	30.89 (8.46-135.07)	0.19 (0.095-0.47)	0.095 (0.0-0.19)	30.51 (7.17-50.33)	27.56 (14.54-45.81)
Abortion	0	1.33 (0.76-6.17)	1.14 (0.47-4.18)	29.08 (11.31-98.85)	23 (13.16-87.30)	0.19 (0.095-0.47)	0.095 (0.0-0.19)	27.66 (9.6-41.44)	27.56 (11.21-47.62)
	1≤	0.85 (0.47-2.37)	1.61 (0.47-3.32)	25.47 (17.96-44.48)	14.16 (8.46-34.69)	0.095 (0.0-0.28)	0.095 (0.0-0.19)	22.14 (4.37-42.77)	21.57 (0.0-36.69)
Number of pregnancy	0	1.33 (0.76-6.65)	1.52 (0.76-4.94)	24.14 (11.31-106.46)	22.33 (14.92-106.46)	0.14 (0.047-0.42)	0 (0.0-0.19)	25.11 (7.31-41.44)	23.28 (3.80-46.15)

Independent variables	As		Se		Cd		Pb	
	Placenta blood	Umbilical cord blood	Placenta blood	Umbilical cord blood	Placenta blood	Umbilical cord blood	Placenta blood	Umbilical cord blood
	Median	Median	Median	Median	Median	Median	Median	Median
	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)	(Q1-Q3)
1 ≤	1.14 (0.66-2.5)	1.14 (0.38-3.18)	29.08 (17.01-54.27)	16.49 (8.46-63.35)	0.14 (0.047-0.28)	0.095 (0.0-0.19)	27.99 (7.50-42.77)	27.56 (11.78-46.15)
Median total	1.28 (0.66-5.03)	1.52 (0.47-3.99)	28.42 (14.92-94.34)	21.29 (10.64-65.49)	0.14 (0.0-0.38)	0.095 (0.0-0.19)	27.56 (7.31-42.77)	26.71 (9.88-45.81)

The total median values in all samples, except As, were observed to be higher in the placental blood rather than the umbilical cord blood. Numerous studies have reported that the amount of Pb, Cd, and As in the umbilical cord blood is lower than the maternal blood (Korpela et al. 1986; Soong et al. 1991; Baranowska 1995; Osman et al. 2000; Sakamoto et al. 2010). Among the studied toxic metals, the ratio of the Cd present in the umbilical cord blood to the placental blood was lower, indicating that the placenta acts as a barrier against Cd transmission and limits the transfer of Cd from the mother to the fetus, which may be due to the metallothionein presents in the placenta (Goyer et al. 1992; Breen et al. 1994). In a study, Tekin et al. (2012) proposed that the difference in placental Pb levels could be influenced by polymorphisms in genes that coded for metallothionein, apparently similar to that of Cd (Tekin et al. 2012).

The US centers for disease control (CDC) have recommended a reference exposure levels of 50, 0.315, and 1 µg/L for Pb, Cd, and As, respectively (Woo et al. 2018). The results of our study showed that 78.48%, 73.81% and 39.29% of pregnant women and 83.53%, 43.53%, and 80% of the umbilical cord samples were below the recommendations of CDC levels for Pb, Cd, and As, respectively. While 21.52%, 26.19%, and 60.71% of maternal blood samples and 16.47%, 56.47%, and 20% of umbilical blood samples were higher than the CDC recommended levels for Pb, Cd and As, respectively.

The presence of toxic metals even at low concentrations in the blood of pregnant women can also damage the fetus (Ha et al. 2009; Lin et al. 2018). Job-related contacts and foods are effective factors in exposure to toxic metals (Martí-Cid et al. 2008). Studies have revealed that approximately 88% of rice consumed in Iran (including Iranian, Pakistani, and Indian brands) does not meet national standards and WHO/FAO guidelines, and the health risks are unacceptable (Sharafi et al. 2019). The risks of As and Pb in the Indian rice and the Cd in Iranian rice are significantly higher than other types. Contamination of the consumed rice can increase the concentration of toxic metals in the maternal blood (Sharafi et al. 2019).

A study in Sabzevar disclosed that the concentration of toxic metals in agricultural products irrigated by effluent wastewater was higher than the maximum permitted level (Mazhari et al. 2019). These toxic metals can enter the food chain through bio-concentration and bio-magnification phenomena (Martí-Cid et al. 2008).

Selenium (Se) is an essential element for the human body. Some authors have reported the range of 60-140 µg/L to be safe for humans (Fairweather-Tait et al. 2011; Llorente Ballesteros et al. 2020). The statistical results of this study showed that the Se concentration levels in 72.5% of the pregnant women were below 60 µg/L, while 27.5% were above this value. Besides, 6% of pregnant women had Se levels higher than 140 µg/L. Table 2 demonstrates the comparison of toxic and essential metals levels in Iran and other countries (Vigeh et al. 2006; Rudge et al. 2009; Sakamoto et al. 2010; Al-Saleh et al. 2011; Ghaemi et al. 2013; Jin et al. 2014; Ettinger et al. 2017; Polanska et al. 2017; Lin et al. 2018; Kobayashi et al. 2019;

Ballesteros et al. 2020). According to this table, the level of Se in pregnant women in this study was very low compared to other countries.

Table 2
The levels of estimated toxic metals in some cities and countries

Country	Cadmium levels µg/L		Lead levels µg/ dL		Arsenic levels µg/L		Selenium levels µg/L		References
	Cord	Maternal	Cord	Maternal	Cord	Maternal	Cord	Maternal	
Iran, Sabzevar	0.095	0.14	26.71	27.56 (µg/L)	1.33	1.23	21.29	28.42	This study
Iran, Tehran*	0.34	0.54	4.30	5.09	-	-	-	-	(Vigeh et al. 2006)
Iran, Shiraz	-	-	-	-	-	-	-	71.22	(Ghaemi et al. 2013)
Poland*	-	-	-	-	-	-	-	48.35	(Polanska et al. 2017)
Saudi Arabia*	0.780	0.986	2.551	2.897	-	-	-	-	(Al-Saleh et al. 2011)
South Africa**	0.02	0.15	1.54	2.3	-	-	-	-	(Rudge et al. 2009)
Japan**	-	-	-	-	-	-	-	170 ^a	(Kobayashi et al. 2019)
Spain, Madrid*	-	-	-	-	-	-	-	73.06	(Ballesteros et al. 2020)
China, Shenqiu*	0.11	-	3.37	-	0.92	-	-	-	(Lin et al. 2018)
Japan, Munakata*	0.22 ^a	1.97 ^a	13.2 ^a	26.4 ^a	3.76 ^a	6.16 ^a	227 ^a	192 ^a	(Sakamoto et al. 2010)
Canada*	-	-	-	-	-	0.6	-	-	(Ettinger et al. 2017)
China, Shanxi**	-	-0.47	-	24.48(µg/L)	-	0.52	-	-	(Jin et al. 2014)
*Geometric mean									
**Median									
^a ng/g									

Investigations have revealed that the amount of Se in the body varies significantly between residents of different countries. This difference is due to the amount of Se in the soil and the intake of Se from the diet (Zachara et al. 2001). Several studies have shown that the concentration of Se in the blood decreases significantly during pregnancy (Lyons et al. 2005; Pieczyńska and Grajeta 2015). The reasons for Se deficiency are included: the transfer of Se to the fetus (Imai et al. 2001), underlying active disease (Navarro-Alarcon and López-Martínez 2000), and a diet containing toxic metals (Navarro-Alarcon and Cabrera-Vique 2008). Se deficiency in pregnant women may lead to dysfunction of the developing fetal nervous system (Cengiz et al. 2004).

3.2. Correlation between the toxic metals

Based on Table 3, the results of the test showed a positive and meaningful correlation between Pb, Hg, Cd, As and Se levels in the blood samples of the placenta and umbilical cord.

Table 3
Correlations of toxic metals in placental blood and umbilical cord blood

	As ^P	As ^U	Se ^P	Se ^U	Cd ^P	Cd ^U	Hg ^P	Hg ^U	Pb ^P	Pb ^U
As ^P	1.000									
As ^U	0.615 (0.001*)	1.000								
Se ^P	0.816 (0.001*)	0.561 (0.001*)	1.000							
Se ^U	0.661 (0.001*)	0.724 (0.001*)	0.661 (0.001*)	1.000						
Cd ^P	0.176 (0.112)	0.111 (0.319)	0.161 (0.152)	0.069 (0.531)	1.000					
Cd ^U	0.080 (0.477)	0.269 (0.013*)	0.104 (0.361)	0.047 (0.665)	0.414 (0.001*)	1.000				
Hg ^P	0.639 (0.001*)	0.558 (0.001*)	0.828 (0.001*)	0.409 (0.002*)	0.435 (0.001*)	0.194 (0.087)	1.000			
Hg ^U	0.539 (0.001*)	0.602 (0.001*)	0.388 (0.004*)	0.931 (0.001*)	0.285 (0.008*)	0.318 (0.003*)	0.627 (0.000*)	1.000		
Pb ^P	0.000 (0.999)	-0.138 (0.229)	-0.220 (0.051)	-0.184 (0.105)	0.461 (0.001*)	0.180 (0.113)	0.491 (0.001*)	0.370 (0.008*)	1.000	
Pb ^U	-0.217 (0.050)	-0.030 (0.780)	-0.256 (0.022*)	-0.211 (0.051)	0.398 (0.002*)	0.410 (0.001*)	0.318 (0.004*)	0.407 (0.001*)	0.654 (0.001*)	1.000
* Statistically Significant Note: P: Placental blood, U: Umbilical cord blood The figures in parentheses refer to p values.										

Many similar studies have shown that Pb, Cd, As, and Hg can pass through the placental barrier (Marques et al. 2007; Ha et al. 2009; Kim et al. 2011; Johnston et al. 2014; Lin et al. 2018; Hadavifar et al. 2019). Moreover, a positive and meaningful correlation was found between the levels of Hg and Cd, Hg and Pb, and Hg and As in the maternal blood and the umbilical cord blood. Another positive and significant correlation was observed between Pb and Cd levels in the maternal blood and the umbilical cord blood. These results are consistent with the studies of Lin et al. 2018 (Lin et al. 2018). The presence of Se in maternal blood prevents many toxins from entering to the fetus (Magos et al. 1980).

Se is a known antagonist of Hg, As, Pb, and Cd (Käkelä et al. 1999; Musik et al. 1999; Lazarus et al. 2011). It has antioxidant properties that reduce the toxicity of toxic metals by forming neutral metal selenide complexes such as CdSe and HgSe (Yang et al. 2002).

According to Table 3 and Figure 2, the results revealed that there was a positive and significant association between Se and Hg ($r=0.82$, $p < 0.001$) and As ($r=0.81$, $p < 0.001$) in the maternal blood (Figure 2-A) and meaningful correlation between Se and

Hg ($r=0.93$, $p<0.001$) and As ($r=0.72$, $p<0.001$) in the umbilical cord blood (Figure 2-B). Earlier studies confirmed the positive and significant correlation between Se and Hg and As levels (1). This association implies that with the increase of toxic metals the umbilical cord absorbs more Se from the maternal blood to decline the toxic metals entering the fetus (Kantola et al. 2000).

The reaction of selenite (Se (IV)) with arsenite (As (III)) is a glutathione-mediated redox reaction that forms a non/less-toxic compound in the body (Sun et al. 2014).

The present study demonstrated a meaningful negative correlation between maternal blood Se level and Pb in the umbilical cord ($r=-0.256$, $p=0.022$), which is similar to that of Bo Xu et al. (1994) (Xu et al. 1994).

3.3. As levels and its association with the independent studied variables

The statistical data of this study in Table 1 showed that the levels of As in analyzed samples of rural areas were higher than the urban areas. In such a way that the As level in the umbilical cord and maternal blood samples in the rural areas was about 3-5 times higher than those in urban areas. Food and water are considered the main sources for As exposure. A study in Bangladesh reported that pregnant women were chronically exposed to a range of natural As compounds in their drinking water (Kwok et al. 2006).

One of the major factors is the absorption of As in the mineral form in rice (Awata et al. 2017). Probably one of the reasons for the high As levels in rural areas could be attributed to the consumption of Indian rice, which is lower-cost than other Iranian rice types due to their weaker economic conditions.

Investigations have shown that the risk of As existing in this type of rice is higher than the other types (Sharafi et al. 2019). The agricultural pesticides can also be effective in exposing rural women to As, which needs further investigation.

The results of univariate linear regression analysis displayed that As level has a significant association with the living area of the pregnant women (Table 4). According to Table 5, the results of multiple linear regression analysis exhibited that the As levels had a meaningful association with the living area of the pregnant women ($p<0.001$), while no significant association was found with other studied variables.

Table 4

Association between toxic metals and independent variables according to univariate linear regression analyses

Independent variables	As		Se		Cd		Pb	
	β^a (95% CI)	P value	β^a (95% CI)	P value	β^a (95% CI)	P value	β^a (95% CI)	P value
Living area (rural)	35.78 (-23.24, 94.82)	0.017	52.38 (33.7, 71.07)	<0.001	-0.16 (-0.45, 0.11)	0.241	-10.84 (-25.11, 3.42)	0.130
Sex (Female)	-0.88 (-2.71, 0.95)	0.342	-10.76 (-32.84, 11.32)	0.335	-0.036 (-0.32, 0.25)	0.804	-8.05 (-22.48, 6.38)	0.271
Filled teeth (1≤)	-22.02 (-82.72, 38.66)	0.470	-23.41 (-45.60, -1.22)	0.038	0.04 (-0.24, 0.34)	0.757	-7.11 (-21.95, 7.72)	0.342
Mother age (25≤)	-26.47 (-85.33, 32.39)	0.373	16.93 (-4.66, 38.52)	0.122	0.14 (-0.13, 0.43)	0.308	5.80 (-8.52, 20.13)	0.422
Abortion (1≤)	-15.72 (-83.92, 52.46)	0.647	-14.4 (-39.11, 10.30)	0.249	-0.14 (-0.47, 0.18)	0.397	-4.98 (-21.23, 11.26)	0.543
Number of pregnancy (1≤)	-32.9 (-92.21, 26.39)	0.272	-8.15 (-30.18, 13.86)	0.463	-0.028 (-0.31, 0.26)	0.845	5 (-9.43, 19.43)	0.492
^a Regression coefficient from univariate linear regression.								

Table 5

Association between toxic metals and independent variables according to multiple linear regression analyses ^a

Independent variables	As		Se		Cd		Pb	
	β^b (95% CI)	P value	β^b (95% CI)	P value	β^b (95% CI)	P value	β^b (95% CI)	P value
Living area (rural)	4.56(3.06, 6.13)	<0.001	47.77(3.83, 45)	<0.001	-0.18(-0.49, 0.12)	0.232	-14.86(-29.98, 0.25)	0.054
Sex (Female)	0.14(-1.49, 1.77)	0.862	7.47(-12.9, 27.85)	0.467	0.02(-0.29, 0.34)	0.893	-4.92(-20.9, 11.07)	0.541
Filled teeth (1≤)	-0.99(-2.7, 0.71)	0.251	-20.49(-42, 1.01)	0.061	-0.05(-0.39, 0.28)	0.742	-11.67(-28.48, 5.13)	0.170
Mother age (25≤)	1.39(-0.27, 3.06)	0.100	24.41(3.83, 45)	0.021	0.2(-0.12, 0.53)	0.224	7.93(-8.31, 24.17)	0.334
Abortion (1≤)	-1.03(-3.04, 0.97)	0.308	-14.5(-39, 10.05)	0.243	-0.15(-0.54, 0.24)	0.447	-6.9(-26.17, 12.37)	0.478
Number of pregnancy (1≤)	-1.38(-3.13, 0.37)	0.121	-13.14(-34.84, 8.56)	0.230	-0.01(-0.35, 0.34)	0.967	7.45(-9.76, 24.67)	0.391
^a Calculated regression coefficients were adjusted for all variables in the table.								
^b Regression coefficients from multiple linear regression model.								

Studies in Canada have also shown a significant association between the levels of As in the blood of Canadian and non-Canadian pregnant women, which shows that the place of residence of pregnant women affects the level of As, which is comparable to the results of the present study. Furthermore, it is reported that there is a meaningful association between the

age of the individuals and the As blood level (Ettinger et al. 2017), but in this study, no significant association was discovered.

3.4. Pb concentration and the association with the independent studied variables

According to Table 1, the results presented that the median of Pb concentration values in rural pregnant women was higher than that in the urban areas. It is proposed that mothers living in rural areas do more outdoor activities. So the higher Pb levels in rural living mothers may be due to the more inhalation dust and particulates. Sabzevar city has been located in an arid area. From other hand, the study of Hosseini et al. (Hosseini et al. 2016) in Iran has demonstrated that dusty and windy days enhances the level of heavy metals in the air and their findings have been significant for Pb levels. Pb blood concentration of pregnant women increased with age. Some studies confirm this claim (Wells et al. 2011). Besides, Pb concentrations were lower in women who had experienced more abortions. The reason for this decrease could be related to the elimination of Pb through abortion. In the pregnancy the mobilization of Pb from maternal bones (as the main source of body Pb) to the fetus enhanced that exposes the fetus to the toxicity and abortion. However this phenomena caused to decrease the maternal Pb levels (Gulson et al. 1997). The results of univariate linear regression showed that none of the studied independent variables had a significant association with the amount of Pb in the pregnant women's blood (Table 4).

The multiple linear regression results, which are brought in Table 5 demonstrated that Pb concentration had a meaningful association with the living area of pregnant women ($p < 0.054$). Al-Saleh et al. (2014) reported that Pb concentration had a significant association with the place of residence of pregnant women (Al-Saleh et al. 2014), which is similar to the results of this study.

3.5. Cd concentration and its association with the studied independent variables

Statistical results revealed no meaningful variation in Cd concentration according to independent variables (Table 1). Additionally, univariate and multiple linear regressions showed no important relation between Cd concentration and the independent variables (Tables 4 and 5).

In a comprehensive study, Johnston et al. (2014) examined 1,027 pregnant women and reported that age, race, and gender of fetus did not significantly affect Cd levels (Johnston et al. 2014). A more recent investigation by Motawei et al. (2015) indicated that the age and the number of filled teeth had a significant association with Cd levels, while the place of residence showed no important relation. Some studies have shown that geographic location plays an important role in the Cd blood level of pregnant women. The difference in Cd levels is mostly due to the existence of steel factories (Lagerkvist et al. 1996) and mines (Reichrtova et al. 1998) in the vicinity of the residences. Furthermore, some studies have noted that urban pollution increases the amount of Cd in the placenta (Falcon et al. 2003).

3.6. Se concentration and its association with the studied independent variables

Se is one of the few elements that are necessary for the normal growth and development of the organs. According to Table 1, the amount of Se in rural pregnant women is about 5 times more than urban pregnant women.

Based on the univariate linear regression results in Table 4, Se levels had a significant association with the living area of pregnant women and the number of filled teeth. The results of multiple linear regression showed that Se concentration had a significant association with the living area ($p < 0.001$) (Table 5). In different areas, the amount of Se in the blood samples of the population changes according to its absorption, which depends on not only the Se content in the soil but also the grains and plants that have grown on the soil (Oldereid et al. 1998).

Studies demonstrated that the serum selenium concentrations in the United States and Canada vary depending on the amount of Se in the soil and the local food consumption. For example, the concentration in the residents of the Midwestern and Western regions of the United States is higher than the Southern and Northeastern regions (Niskar et al.; Kafai and Ganji 2003). A study by Pettigrew et al. (2019) displayed that the amount of Se in the meat and egg yolk of the chickens bred in the rural areas was higher than those of which were sold in urban food stores. They suggested that rural chickens may collect Se while they are free to scratch the ground and eat insects and other foods (Pettigrew et al. 2019). Similarly, it seems that in this study, rural pregnant women have higher access to Se-rich resources than urban women do.

4. Conclusion

Present study arguing about the toxic metal burdens in maternal and fetus blood samples taken from women referred to Shahidan Mobini Hospital for delivery. As our findings showed, 78.48%, 73.81% and 39.29% of maternal blood samples and 83.53%, 43.53%, and 80% of the umbilical cord blood samples were below the recommendations of CDC levels for Pb, Cd, and As, respectively. The results also revealed that there was a positive and meaningful correlation between Se and Hg ($r=0.82$, $p<0.001$) and As ($r=0.81$, $p<0.001$) in the maternal blood and meaningful correlation between Se and Hg ($r=0.93$, $p<0.001$) and As ($r=0.72$, $p<0.001$) in the umbilical cord blood samples.

According to the scientific reports, the range of 60-140 $\mu\text{g/L}$ of selenium is safe for humans. Whereas, the statistical results of this study showed that the Se concentration levels in 72.5% of the pregnant women were below 60 $\mu\text{g/L}$ and only 6% of pregnant women had Se levels higher than 140 $\mu\text{g/L}$. Finally, we find that Pb and As concentration values in rural pregnant women were higher than mothers living in urban areas.

Pieces of evidence implying that the drinking water of Sabzevar may be the main risk factor posing the residents to toxic metals duo to chromium mining in watershed and drainage basin supplying fresh water for Sabzevar society. Moreover, using inadequately treated municipal wastewater for agricultural products is the other risk factor that these two risk factors will be investigated more in our future studies.

Declarations

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Conflicts of interest/Competing interests

The authors declare that they have no conflict of interest.

Availability of data and material

Not applicable.

Code availability

Not applicable.

Ethics approval

Ethical approval taken from the Ethics Committee of Sabzevar University of Medical Sciences (IR.MEDSAB.REC.1395.67).

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Author contributions

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Ali Kazemi: ICP OES analysis, sample preparation

References

1. Al-Saleh I, Shinwari N, Mashhour A et al (2011) Heavy metals (lead, cadmium and mercury) in maternal, cord blood and placenta of healthy women. *Int J Hyg Environ Health* 214:79–101. doi: 10.1016/j.ijheh.2010.10.001
2. Al-Saleh I, Shinwari N, Mashhour A, Rabah A (2014) 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. doi: 10.1016/j.ijheh.2013.04.009
3. Awata H, Linder S, Mitchell LE, Delclos GL (2017) Association of dietary intake and biomarker levels of arsenic, cadmium, lead, and mercury among Asian populations in the United States: NHANES 2011–2012. *Environ Health Perspect* 125:314–323
4. Ballesteros MTL, Barrado BG, Serrano IN et al (2020) Evaluation of blood mercury and serum selenium levels in the pregnant population of the Community of Madrid, Spain. *J Trace Elem Med Biol* 57:60–67
5. Baranowska I (1995) Lead and cadmium in human placentas and maternal and neonatal blood (in a heavily polluted area) measured by graphite furnace atomic absorption spectrometry. *Occup Environ Med* 52:229–232
6. Bellinger D, Leviton A, Needleman HL et al (1986) Low-level lead exposure and infant development in the first year. *Neurobehav Toxicol Teratol* 8:151–161
7. Borja-Aburto VH, Hertz-Picciotto I, Lopez MR et al (1999) Blood lead levels measured prospectively and risk of spontaneous abortion. *Am J Epidemiol* 150:590–597
8. Breen JG, Eisenmann C, Horowitz S, Miller RK (1994) Cell-specific increases in metallothionein expression in the human placenta perfused with cadmium. *Reprod Toxicol* 8:297–306
9. Butler Walker J, Houseman J, Seddon L et al (2006) Maternal and umbilical cord blood levels of mercury, lead, cadmium, and essential trace elements in Arctic Canada. *Environ Res* 100:295–318. doi: 10.1016/j.envres.2005.05.006
10. Cengiz B, Söylemez F, Öztürk E, Çavdar AO (2004) Serum zinc, selenium, copper, and lead levels in women with second-trimester induced abortion resulting from neural tube defects. *Biol Trace Elem Res* 97:225–235
11. Ettinger AS, Arbuckle TE, Fisher M et al (2017) Arsenic levels among pregnant women and newborns in Canada: results from the Maternal-Infant Research on Environmental Chemicals (MIREC) cohort. *Environ Res* 153:8–16

12. Fairweather-Tait SJ, Bao Y, Broadley MR et al (2011) Selenium in human health and disease. *Antioxid Redox Signal* 14:1337–1383
13. Faita F, Cori L, Bianchi F, Andreassi M (2013) Arsenic-induced genotoxicity and genetic susceptibility to arsenic-related pathologies. *Int J Environ Res Public Health* 10:1527–1546
14. Falcon M, Vinas P, Perez-Carceles MD, Luna A (2003) Placental cadmium and lipid peroxidation in smoking women related to newborn anthropometric measurements. *Arch Environ Contam Toxicol* 45:278–282
15. García-Esquinas E, Pérez-Gómez B, Fernández-Navarro P et al (2013) Lead, mercury and cadmium in umbilical cord blood and its association with parental epidemiological variables and birth factors. *BMC Public Health* 13:841
16. Ghaemi SZ, Forouhari S, Dabbaghmanesh MH et al (2013) A prospective study of selenium concentration and risk of preeclampsia in pregnant Iranian women: a nested case–control study. *Biol Trace Elem Res* 152:174–179
17. Ghasemi SS, Hadavifar M, Maleki B, Mohammadnia E (2019) Adsorption of mercury ions from synthetic aqueous solution using polydopamine decorated SWCNTs. *J Water Process Eng* 32:100965. doi: <https://doi.org/10.1016/j.jwpe.2019.100965>
18. Goyer RA, Haust MD, Cherian MG (1992) Cellular localization of metallothionein in human term placenta. *Placenta* 13:349–355
19. Gulson BL, Jameson CW, Mahaffey KR et al (1997) Pregnancy increases mobilization of lead from maternal skeleton. *J Lab Clin Med* 130:51–62. doi: 10.1016/s0022-2143(97)90058-5
20. Ha M, Kwon H-J, Lim M-H et al (2009) Low blood levels of lead and mercury and symptoms of attention deficit hyperactivity in children: a report of the children's health and environment research (CHEER). *Neurotoxicology* 30:31–36
21. Hadavifar M, Rastakhiz M, Souvizi B et al (2019) Biomonitoring of maternal and fetal exposure to mercury in Sabzevar and its affecting risk factors. *J Hazard Mater* doi. 10.1016/j.jhazmat.2019.121781
22. Hernandez-Avila M, Peterson KE, Gonzalez-Cossio T et al (2002) Effect of maternal bone lead on length and head circumference of newborns and 1-month-old infants. *Arch Environ Heal An Int J* 57:482–488
23. Hinwood AL, Callan AC, Ramalingam M et al (2013) Cadmium, lead and mercury exposure in non smoking pregnant women. *Environ Res* 126:118–124. doi: 10.1016/j.envres.2013.07.005
24. Hosseini G, Teymouri P, Giahi O, Maleki A (2016) Health Risk Assessment of Heavy Metals in Atmospheric PM10 in Kurdistan. University of Medical Sciences Campus
25. Iijima K, Otake T, Yoshinaga J et al (2007) Cadmium, lead, and selenium in cord blood and thyroid hormone status of newborns. *Biol Trace Elem Res* 119:10–18
26. Imai H, Suzuki K, Ishizaka K et al (2001) Failure of the expression of phospholipid hydroperoxide glutathione peroxidase in the spermatozoa of human infertile males. *Biol Reprod* 64:674–683
27. Jedrychowski W, Jankowski J, Flak E et al (2006) Effects of Prenatal Exposure to Mercury on Cognitive and Psychomotor Function in One-Year-Old Infants: Epidemiologic Cohort Study in Poland. *Ann Epidemiol* 16:439–447. doi: 10.1016/j.annepidem.2005.06.059
28. Jin L, Liu J, Ye B, Ren A (2014) Concentrations of selected heavy metals in maternal blood and associated factors in rural areas in Shanxi Province, China. *Environ Int* 66:157–164
29. Jin L, Zhang L, Li Z et al (2013) Placental concentrations of mercury, lead, cadmium, and arsenic and the risk of neural tube defects in a Chinese population. *Reprod Toxicol* 35:25–31
30. Jin Y, Xi S, Li X et al (2006) Arsenic speciation transported through the placenta from mother mice to their newborn pups. *Environ Res* 101:349–355
31. Johnston JE, Valentiner E, Maxson P et al (2014) Maternal cadmium levels during pregnancy associated with lower birth weight in infants in a North Carolina cohort
32. Kafai MR, Ganji V (2003) Sex, age, geographical location, smoking, and alcohol consumption influence serum selenium concentrations in the USA: Third National Health and Nutrition Examination Survey, 1988-1994. *J Trace Elem Med Biol*

33. Käkälä R, Käkälä A, Hyvärinen H (1999) Effects of nickel chloride on reproduction of the rat and possible antagonistic role of selenium. *Comp Biochem Physiol Part C Pharmacol Toxicol Endocrinol* 123:27–37
34. Kantola M, Purkunen R, Kröger P et al (2000) Accumulation of cadmium, zinc, and copper in maternal blood and developmental placental tissue: differences between Finland, Estonia, and St. Petersburg. *Environ Res* 83:54–66
35. Kennedy DA, Woodland C, Koren G (2012) Lead exposure, gestational hypertension and pre-eclampsia: a systematic review of cause and effect. *J Obstet Gynaecol (Lahore)* 32:512–517
36. Kim B-M, Lee B-E, Hong Y-C et al (2011) Mercury levels in maternal and cord blood and attained weight through the 24 months of life. *Sci Total Environ* 410:26–33
37. Kobayashi S, Kishi R, Saijo Y et al (2019) Association of blood mercury levels during pregnancy with infant birth size by blood selenium levels in the Japan Environment and Children's Study: A prospective birth cohort. *Environ Int* 125:418–429
38. Korpela H, Loueniva R, Yrjänheikki E, Kauppila A (1986) Lead and cadmium concentrations in maternal and umbilical cord blood, amniotic fluid, placenta, and amniotic membranes. *Am J Obstet Gynecol* 155:1086–1089
39. Kwok RK, Kaufmann RB, Jakariya M (2006) Arsenic in drinking-water and reproductive health outcomes: a study of participants in the Bangladesh Integrated Nutrition Programme. *J Heal Popul Nutr* 24:190–205
40. Lagerkvist BJ, Sandberg S, Frech W et al (1996) Is placenta a good indicator of cadmium and lead exposure? *Arch Environ Heal An Int J* 51:389–394
41. Lazarus M, Orct T, Aladrović J et al (2011) Effect of selenium pre-treatment on antioxidative enzymes and lipid peroxidation in Cd-exposed suckling rats. *Biol Trace Elem Res* 142:611–622
42. Li H, Huang K, Jin S et al (2019) Environmental cadmium exposure induces alterations in the urinary metabolic profile of pregnant women. *Int J Hyg Environ Health* 222:556–562. doi: 10.1016/j.ijheh.2019.02.007
43. Lin Z, Chen X, Xi Z et al (2018) Individual heavy metal exposure and birth outcomes in Shenqiu county along the Huai River Basin in China. *Toxicol Res (Camb)* 7:444–453
44. Linn S, Schoenbaum S (1984) The relationship between prenatal exposure to lead and congenital anomalies. *JAMA* 251:2956–2959
45. Llorente Ballesteros MT, García Barrado B, Navarro Serrano I et al (2020) Evaluation of blood mercury and serum selenium levels in the pregnant population of the Community of Madrid, Spain. *J Trace Elem Med Biol* 57:60–67. doi: 10.1016/j.jtemb.2019.09.008
46. Lyons GH, Judson GJ, Ortiz-Monasterio I et al (2005) Selenium in Australia: selenium status and biofortification of wheat for better health. *J Trace Elem Med Biol* 19:75–82
47. Magos L, Webb M, Clarkson TW (1980) The interactions of selenium with cadmium and mercury. *CRC Crit Rev Toxicol* 8:1–42
48. Marques RC, Dórea JG, Bastos WR et al (2007) Maternal mercury exposure and neuro-motor development in breastfed infants from Porto Velho (Amazon), Brazil. *Int J Hyg Environ Health* 210:51–60
49. Martí-Cid R, Llobet JM, Castell V, Domingo JL (2008) Dietary intake of arsenic, cadmium, mercury, and lead by the population of Catalonia, Spain. *Biol Trace Elem Res* 125:120–132
50. Mazhari SA, Abhari A, Mazhari SN (2019) Geochemical and environmental investigation of sewage-irrigated soils and crops of Sabzevar, NE of Iran. *SN Appl Sci* 1:1065
51. McAleer MF, Tuan RS (2001) Metallothionein overexpression in human trophoblastic cells protects against cadmium-induced apoptosis. *Vitr Mol Toxicol A J Basic Appl Res* 14:25–42
52. Mohammadnia E, Hadavifar M, Veisi H (2019) Kinetics and thermodynamics of mercury adsorption onto thiolated graphene oxide nanoparticles. *Polyhedron* 173:114139. doi: <https://doi.org/10.1016/j.poly.2019.114139>

53. Musik I, Koziol-Montewka M, Toś-Luty S et al (1999) Immunomodulatory effect of selenosemicarbazides and selenium inorganic compounds, distribution in organs after selenium supplementation. *Biometals* 12:375–382
54. Navarro-Alarcon M, Cabrera-Vique C (2008) Selenium in food and the human body: a review. *Sci Total Environ* 400:115–141
55. Navarro-Alarcon M, López-Martínez MC (2000) Essentiality of selenium in the human body: relationship with different diseases. *Sci Total Environ* 249:347–371
56. Nishijo M, Nakagawa H, Honda R et al (2002) Effects of maternal exposure to cadmium on pregnancy outcome and breast milk. *Occup Environ Med* 59:394–397
57. Nishijo M, Tawara K, Honda R et al (2004) Relationship between newborn size and mother's blood cadmium levels, Toyama, Japan. *Arch Environ Heal An Int J* 59:22–25
58. Niskar AS, Paschal DC, Kieszak SM et al Serum selenium levels in the US population: Third National Health and Nutrition Examination Survey, 1988-1994.
59. Oldereid NB, Thomassen Y, Purvis K (1998) Selenium in human male reproductive organs. *Hum Reprod* 13:2172–2176
60. Oskarsson A, Widell A, Olsson M, Grawé KP (2004) Cadmium in food chain and health effects in sensitive population groups. *Biometals* 17:531–534
61. Osman K, Åkesson A, Berglund M et al (2000) Toxic and essential elements in placentas of Swedish women. *Clin Biochem* 33:131–138
62. Pan J, Song H, Pan XC (2007) Reproductive effects of occupational exposure to mercury on female workers in China: a meta-analysis
63. Pettigrew SM, Pan WK, Berky A et al (2019) In urban, but not rural, areas of Madre de Dios, Peru, adoption of a Western diet is inversely associated with selenium intake. *Sci Total Environ* 687:1046–1054. doi: 10.1016/j.scitotenv.2019.05.484
64. Pieczyńska J, Grajeta H (2015) The role of selenium in human conception and pregnancy. *J trace Elem Med Biol* 29:31–38
65. Polanska K, Hanke W, Krol A et al (2017) Micronutrients during pregnancy and child psychomotor development: Opposite effects of Zinc and Selenium. *Environ Res* 158:583–589
66. Ramon R, Ballester F, Aguinagalde X et al (2009) Fish consumption during pregnancy, prenatal mercury exposure, and anthropometric measures at birth in a prospective mother-infant cohort study in Spain-. *Am J Clin Nutr* 90:1047–1055
67. Reichrtova E, Ursinyova M, Palkovicova L, Wsolova L (1998) Contents and localization of heavy metals in human placentae. *Fresenius J Anal Chem* 361:362–364
68. Rudge CV, Röllin HB, Nogueira CM et al (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
69. Sakamoto M, Man Chan H, Domingo JL et al (2012) Changes in body burden of mercury, lead, arsenic, cadmium and selenium in infants during early lactation in comparison with placental transfer. *Ecotoxicol Environ Saf* 84:179–184. doi: 10.1016/j.ecoenv.2012.07.014
70. Sakamoto M, Murata K, Kubota M et al (2010) Mercury and heavy metal profiles of maternal and umbilical cord RBCs in Japanese population. *Ecotoxicol Environ Saf* 73:1–6. doi: 10.1016/j.ecoenv.2009.09.010
71. Satarug S, Garrett SH, Sens MA, Sens DA (2009) Cadmium, environmental exposure, and health outcomes. *Environ Health Perspect* 118:182–190
72. Sharafi K, Yunesian M, Nodehi RN et al (2019) A systematic literature review for some toxic metals in widely consumed rice types (domestic and imported) in Iran: human health risk assessment, uncertainty and sensitivity analysis. *Ecotoxicol Environ Saf* 176:64–75
73. Soong YK, Tseng R, Liu C, Lin PW (1991) Lead, cadmium, arsenic, and mercury levels in maternal and fetal cord blood. *J Formos Med Assoc Taiwan yi zhi* 90:59–65

74. Sun H-J, Rathinasabapathi B, Wu B et al (2014) Arsenic and selenium toxicity and their interactive effects in humans. *Environ Int* 69:148–158
75. Tekin D, Kayaaltı Z, Aliyev V, Söylemezoğlu T (2012) The effects of metallothionein 2A polymorphism on placental cadmium accumulation: is metallothionein a modifying factor in transfer of micronutrients to the fetus? *J Appl Toxicol* 32:270–275
76. Thompson J, Bannigan J (2008) Cadmium: toxic effects on the reproductive system and the embryo. *Reprod Toxicol* 25:304–315
77. Vige M, Yokoyama K, Ramezanzadeh F et al (2006) Lead and other trace metals in preeclampsia: a case–control study in Tehran, Iran. *Environ Res* 100:268–275
78. Walvekar RR, Kane SV, Nadkarni MS et al (2007) Chronic arsenic poisoning: a global health issue—a report of multiple primary cancers. *J Cutan Pathol* 34:203–206
79. Wells EM, Jarrett JM, Lin YH et al (2011) Body burdens of mercury, lead, selenium and copper among Baltimore newborns. *Environ Res* 111:411–417. doi: 10.1016/j.envres.2010.12.009
80. Woo MK, Young ES, Mostofa MG et al (2018) Lead in Air in Bangladesh: Exposure in a Rural Community with Elevated Blood Lead Concentrations among Young Children. *Int J Environ Res Public Health*. doi: 10.3390/ijerph15091947
81. Xu B, Chia S-E, Ong C-N (1994) Concentrations of cadmium, lead, selenium, and zinc in human blood and seminal plasma. *Biol Trace Elem Res* 40:49–57
82. Yang L, Wang W, Hou S et al (2002) Effects of selenium supplementation on arsenism: an intervention trial in Inner Mongolia. *Environ Geochem Health* 24:359–374
83. Zachara BA, Pawluk H, Korenkiewicz J, Skok Ż (2001) Selenium levels in kidney, liver and heart of newborns and infants. *Early Hum Dev* 63:103–111

Figures

Figure 1

The geographical location of Sabzevar city including its satellite rural areas.

Figure 2

Correlation between Se and Hg and As in the placental blood (A) and Se and Hg and As in the umbilical cord blood (B) (P: Placental blood, U: Umbilical cord blood).