



# Prenatal exposure to chromium (Cr) and nickel (Ni) in a sample of Iranian pregnant women: urinary levels and associated socio-demographic and lifestyle factors

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## Abstract

Heavy metals have been well documented to pose detrimental health effects. The current study aimed to measure the concentration of chromium (Cr) and nickel (Ni) in urinary samples of Iranian pregnant females and determine their potential correlations with different lifestyle variables. The study was conducted in 2019–2020 in Isfahan, Iran, and the urine samples were collected from 140 pregnant women. The concentrations of Cr and Ni in the urinary samples were measured by inductively coupled plasma optical emission spectrometry (ICP-OES). Data on socio-demographic characteristics, use of cleaning products, and lifestyle profiles was collected by validated questionnaires. Cr and Ni were detected in 100% of urinary samples with the mean concentration of  $4.1 \pm 3.4$  and  $7.5 \pm 4.8$   $\mu\text{g/g}$  creatinine, respectively. Significant associations were found between the mean concentration of Cr and Ni with using cooking utensils made of copper, aluminum, Teflon, steel, and enameled, as well as with cosmetic use, and second-hand smoking exposure during pregnancy. The results also showed that the mean urinary Ni and Cr concentrations were significantly different among individuals who consumed seafood and canned food ( $p$ -value  $< 0.05$ ). Furthermore, the mean of urinary Cr and Ni concentrations at high levels of physical activity and scratched utensils used was significantly different from the other categories ( $p$ -value  $< 0.05$ ). According to our findings, the lifestyle determinants and cosmetic products had superiority to socio-demographic characteristics in predicting urinary heavy metals in Iranian pregnant women.

**Keywords** Chromium · Nickel · Heavy metals · Pregnancy · Lifestyle · Socio-demographic

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## Introduction

Heavy metals are highly toxic and may persist in the environment for a long period of time. Several lines of evidence show that humans can be exposed to heavy metals through various routes such as contaminated water and food consumption, polluted air inhalation, smoking, and use of cleaning and cosmetic products (Li et al. 2017; Mohammadi et al. 2019a, b; Shams et al. 2020; Shokoohi et al. 2020). Exposure to these toxic elements has been demonstrated to result in serious health effects, even at trace concentrations. A substantial part of heavy metals may have natural origin, but due to their widespread applications in several industries, including but not limited to food industries, humans might be exposed to various forms of these life-threatening compounds.

Among several well-known heavy metals, nickel and chromium are two important elements frequently added to food as dietary supplements (Pigłowski 2018; Spencer and Palmer 2021). Based on the published knowledge, chromium is found mainly in two forms, hexavalent (Cr(VI)) and trivalent (Cr<sup>3+</sup>),

where a minor quantity of  $\text{Cr}^{3+}$  has been assumed to be essential for human health. However, on the contrast, exposure to Cr (VI), principally via inhalation, has been associated with adverse health impacts, especially respiratory problems (Berardi et al. 2015; Morais et al. 2012). Of particular note, due to its carcinogenicity in humans, Cr (VI) has been classified as Group I human carcinogen by the IARC (International Agency for Research on Cancer) and Group A inhalation carcinogen by the US EPA (Zheng Li et al. n.d.). Nickel (Ni), another naturally occurring element, exists in several forms and has been reported in soil, water, food, and air. Previous studies have shown that humans are exposed to several forms of Ni during daily life, which is assumed to be associated with an elevated risk for some cancers (McDermott et al. 2015).

Similar to Cr, exposure to Ni can occur through food ingestion; however, it may also happen by inhalation, consuming contaminated groundwater, and dermal absorption by contact with jewelry or metallic goods (Briffa et al. 2020; Kumar et al. 2021). Furthermore, nickel has been linked to combustion products and reported in particulate matter (PM) in ambient air (Corbin et al. 2018; Gangwar et al. 2019). Collectively, apart from the abovementioned health effects, there is a large body of evidence demonstrating that exposure to heavy metal can also affect oxidative cell stress, result in nervous system damage, and interfere with glucose metabolism and endocrine disruption (Fu and Xi 2020; Rehman et al. 2018).

Although exposure to heavy metals can negatively affect the health of all age groups, pregnant women are assumed as one of the population groups most vulnerable to these toxic elements. Several previous studies have reposted chemical materials such as benzene (Amin et al. 2018b), bisphenol (Amin et al. 2019a), nitrate (Darvishmotevalli et al. 2019b; Moradnia 2019), paraben (Amin et al. 2018b; Fadaei et al. 2021; Hajizadeh et al. 2020; Hajizadeh et al. 2021), and phthalate (Amin et al. 2019a; Darvishmotevalli et al. 2021), and also heavy metals (Kumar and Mukherjee 2021; Li et al. 2021) in amniotic fluid and cord blood, demonstrating that these toxic metals can easily cross the placenta and reach the growing fetus. Therefore, significant concerns have been raised regarding the adverse effects of maternal exposure to these toxic elements on fetus growth, probably by altering the homeostatic and metabolic mechanisms (Magnusson et al. 2019). This notion is more evident, as maternal exposure to heavy metals has been correlated with increased adverse pregnancy effects (Quansah et al. 2015). There are also several epidemiological studies that have confirmed the association between prenatal chemical pollutant exposure and increased adverse pregnancy outcomes (Darvishmotevalli et al. 2019b; Guo et al. 2010; McDermott et al. 2015). However, since environmental hazards are unequally distributed throughout societies and lifestyle and socio-demographic factors differ among different populations, pregnant women in developing

countries, like Iran, may experience a greater burden of exposure to these toxic heavy metals and subsequent detrimental health effects (Darvishmotevalli et al. 2019; Pope et al. 2016). To the best of our knowledge, no documents have evaluated the urinary levels of nickel and chromium in Iranian pregnant women with regard to their lifestyle and socio-demographic variables. Thus, in this research, we aimed to evaluate the concentrations of two important heavy metals, i.e., Cr and Ni, in urine samples of pregnant females and their potential associations with lifestyle and socio-demographic factors.

## Materials and methods

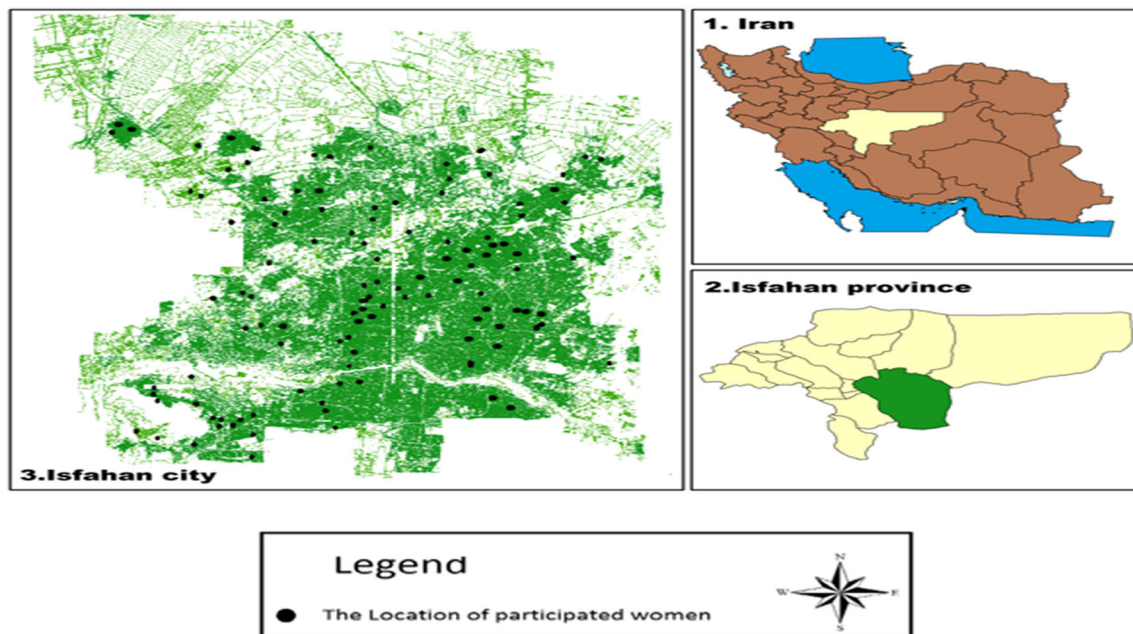
### Study population

This cross-sectional study was conducted on 140 pregnant women in their first trimester in Isfahan, Iran, between the years 2019 and 2020. The participants were selected randomly and the spatial distribution of their location of residence is shown in Fig. 1. The objectives, procedure, and also voluntary nature of the study were clearly explained to the participants and a signed consent letter was taken from them. Of note, the ethical issues linked to this study were approved by the ethics committees of Isfahan University of Medical Sciences.

The early morning spot urine samples were collected in borosilicate containers and then transferred to the laboratory to be kept at  $-20^{\circ}\text{C}$ . The validated questionnaires (PERSIAN Birth Cohort questionnaires) were utilized to collect information about socio-demographic determinants (maternal age, family income, education level, maternal occupation), lifestyle variables (pre-pregnancy BMI, physical activity, smoking habit, and food habits (seafood and canned food consumption)), type of utensils for cooking (zinc, copper, aluminum, enameled, Teflon, cast iron, steel, and Pyrex), use of scratched utensils for cooking, household cleaning, and cosmetic product usage. The IPAQ (International Physical Activity Questionnaire) was utilized to evaluate total physical activity (MET-min/week) score (Cleland et al. 2018). The FFQ (Food Frequency Questionnaire) was applied to gather data about the food intake habits of participants (Poustchi et al. 2018).

### Measuring urinary heavy metals

The frozen urine samples were completely thawed at room temperature and then homogenized. A total of 3.0 mL of urine was poured into a polypropylene tube containing 15  $\mu\text{L}$  of 65% (v/v)  $\text{HNO}_3$  and then stored in a refrigerator at  $5^{\circ}\text{C}$ . It should be mentioned that, approximately 2 h before the preparation of samples, the urine samples were brought to room temperature. One milliliter of the sample was pipetted into a 10-mL polypropylene tube and filled up to 5.0 mL with 1.2%



**Fig. 1** The distribution of the individuals living in Isfahan city

(v/v)  $\text{HNO}_3$  (Feng et al. 2015). Finally, the prepared solution was injected into the ICP-OES (Varian 720/730-ES) to measure the concentration of heavy metals.

Heavy metal concentrations were adjusted using creatinine amount to minimize the bias of the dilution difference between urine samples. The limits of detection (LOD) were 0.15 and 0.3  $\mu\text{g/L}$  for Cr and Ni, respectively.

### Analysis of data

Continuous determinants have been reported as mean  $\pm$  SD, minimum, and maximum, whereas categorical variables as frequencies (percent). The Kolmogorov-Smirnov test and Q-Q plot were utilized to specify the normality of continuous data. Appropriate transformation approaches were applied for those heavy metal concentrations with abnormal distribution. Independent samples *t*-test or analysis of variance (ANOVA) was utilized to compare the mean of heavy metal concentrations across categories of possible lifestyle and demographic variables. The Bonferroni post hoc test was used to determine differences between categories after rejecting the null hypothesis in the analysis of variance. All statistical analyses were conducted by SPSS software (IBM SPSS Inc., Chicago, IL, version 23). A *p*-value less than 0.05 was considered statistically significant.

### Results and discussion

The characteristics of the studied individuals are given in Table 1. According to the findings, 45.7% ( $n = 64$ ) were under 30 years old, 54.3% ( $n = 76$ ) were 30 years old, 57.1% of

females ( $n = 80$ ) were overweight, 38.6% ( $n = 54$ ) were normal weight, and only 4.3% of women ( $n = 6$ ) were underweight. Majority of the participants had an academic education ( $n = 116$ , 82.8%). Eighty percent of pregnant women were householder ( $n = 112$ ) and 63.6% of the total population ( $n = 89$ ) were classified into the middle-income group.

The findings also indicated that more than 50% of individuals were categorized into the low consumers of canned food ( $n=81$ ) and seafood ( $n=74$ ). Additionally, 50% of females used Teflon containers for cooking, whereas Pyrex ( $n=7$ , 5%) and enameled ( $n=12$ , 8.6%) containers were used less frequently. Steel, zinc, cast iron, copper, and aluminum were the most commonly used materials for cooking food after Teflon. In addition, more than half of the participants ( $n=79$ , 56.4%) declared that they used scratched utensils for cooking.

Based on the initial results, household cleaning and cosmetic products were respectively used by 100% (140) and 62.85% ( $n=88$ ) of individuals. None of the pregnant women was smokers; however, about 50.75% ( $n=71$ ) were identified as passive smokers.

A large number of participants were classified as low ( $n=53$ , 37.9%) or middle ( $n=55$ , 39.3%) physical activity group, but 22.9% ( $n=32$ ) were assigned to the heavy physical activity group ( $n=32$ ).

In the current study, the normalization of data was performed by using the Cox-box method. The mean, quartile, maximum, and minimum of creatinine-adjusted heavy metal concentration are reported in Table 2. Accordingly, Ni and Cr were detected in 100% of urine samples ( $n=140$ ). The lowest and highest concentrations were 0.5  $\mu\text{g/g}$  creatinine and 33.3  $\mu\text{g/g}$  creatinine for Ni and 0.17  $\mu\text{g/g}$  creatinine and 33  $\mu\text{g/g}$  creatinine for Cr.

**Table 1** The characteristics of the studied pregnant women

Variables	Categories	n (%)	
Maternal age (years)	<25	16 (11.4)	
	25–29	48 (34.3)	
	30–34	52 (37.2)	
	>34	24 (17.1)	
Pre-pregnancy BMI (kg/m <sup>2</sup> )	Underweight (<18.5)	6 (4.3)	
	Normal weight (18.5–23.9)	54 (38.6)	
	Overweight (≥24)	80 (57.1)	
Education level	Academic	116 (82.8)	
	High school	18 (12.9)	
	Less than high school	6 (4.3)	
Family income	Low	43 (30.7)	
	Middle	89 (63.6)	
	High	8 (5.7)	
Maternal occupation	Householder	112 (80)	
	Employed	28 (20)	
Used scratched utensils	No	61 (43.6)	
	Yes	79 (56.4)	
Seafood consumption	Low (1 per month)	74 (52.9)	
	Middle (2–4 per month)	49 (35)	
	High (>4 per week)	17 (12.1)	
Canned food consumption	Low (1 per month)	81 (57.9)	
	Middle (2–4 per month)	39 (27.9)	
	High (>4 per week)	20 (14.3)	
Used utensils for cooking	Zinc	No	90 (64.3)
		Yes	50 (35.7)
	Copper	No	115 (82.2)
		Yes	25 (17.8)
	Aluminum	No	117 (83.6)
		Yes	23 (16.4)
	Enameled	No	128 (91.4)
		Yes	12 (8.6)
	Teflon	No	70 (50)
		Yes	70 (50)
	Cast Iron	No	92 (65.7)
		Yes	48 (34.3)
	Steel	No	83 (59.3)
		Yes	57 (40.7)
	Pyrex	No	133 (95)
		Yes	7 (5)
	Cosmetic usage	Yes	88 (62.85)
		No	52 (37.15)
	Household cleaning product usage	Yes	140 (100)
		No	0 (0)
	Smoking	Yes	0 (0)
		No	140 (100)
	Passive smoking	Yes	71 (50.75)
		No	69 (49.28)
Physical activity	Low	53 (37.9)	
	Moderate	55 (39.3)	
	High	32 (22.9)	

The mean value of Ni and Cr was found to be 4.1±3.4 3 µg/g creatinine and 7.5±4.8 µg/g creatinine, respectively, which was approximately greater than those values reported by other studies (Fort et al. 2014; Rocha et al. 2016). The conflict in these findings can be explained by the different characteristics of the studied population, as well as different lifestyle and socio-demographic variables among the target groups. But, in line with our findings, previous studies showed that the serum concentrations of heavy metals among individuals from low- and middle-income group (developing societies) are

much higher than those reported in developed countries (Orisakwe et al. 2012; Weidenhamer et al. 2014).

The distribution of Cr and Ni concentrations in relation to some influencing determinants such as education level, family income, occupation status, consumption of seafood and canned foods, use of various types of cooking containers (zinc, copper, aluminum, enameled, Teflon, cast iron, steel, and Pyrex) and scratched utensils, household cleaning products and cosmetic use, smoking and passive smoking habit, and physical activity is presented in Table 3.

Based on the results, the mean of urinary Cr and Ni concentrations did not show significant differences in the levels of maternal education ( $p$ -value  $> 0.05$ ). Similarly, research conducted among pregnant women in Myanmar revealed no significant difference between maternal education status and levels of urinary heavy metals (Wai et al. 2017). In contrast, a study conducted in China showed that females with higher level of education had a lower concentrations of urinary Cd, Ni, and Pb (Chang et al. 2016). Controversial effects of maternal education on urinary levels of investigated heavy metals in different studies may be rooted in the fact that, while maternal education is a significant factor, education influence strongly adhered to sociocultural factors (DiBenedetto and Schunk 2018).

As revealed, around 90% of the studied pregnant females were categorized into the low- to middle-income group, although no significant difference was seen between family income and urinary Cr and Ni concentrations ( $p$ -value  $> 0.05$ ).

Parallel results were also demonstrated by Zeng et al. (2019) and Zaw and Taneepanichskul (2019). However, some reports have shown that family income was positively correlated with urinary heavy metals such as Cr, Cd, As, and Hg among pregnant females (Lin et al. 2018). As justified for education, the effect of family income on urinary heavy metal concentration can be mediated by various cultural and socioeconomic factors. Meanwhile, family income, education level, and other sociocultural factors are somehow interlinked; thus, they can have different effects in developed societies compared with developing countries (Wenzel et al. 2018).

Occupational exposure is often introduced as a risk factor for women's fertility and [pre-term delivery](#) (Amadi et al. 2017). The results of the present study show that the mean concentration of urinary Cr and Ni was not statically different between females who were householders and employees ( $p$ -value  $> 0.05$ ). However, some previous documents have revealed a positive correlation between heavy metal occupational exposure and increased risk of neonatal outcome. The study conducted in China indicated abortion incidence correlated with occupational Cr. In fact, the incidence rate of abortion was elevated by 6% for feminine workers with occupational Cr exposure (Yang et al. 2013). Besides, recent research performed in Nigeria indicates that the miscarriage incidence increased by 1.6% in females exposed to Cr (Amadi et al. 2017).

The mean urinary Cr and Ni concentrations showed significant differences in the levels of the used utensils, i.e., copper, aluminum, Teflon, steel, and enameled ( $p$ -value  $< 0.05$ ). It must be noted that when the used utensils are scratched, the risk of leaching heavy metals increases. This becomes more evident as a significant difference was observed between the mean concentrations of Ni and Cr when individuals utilized scratched utensils for cooking.

In parallel with our findings, the result of Ojezele et al. also indicated that Ni, Cr, and Pb with values of  $0.89 \pm 0.26$  mg/L,  $0.28 \pm 0.13$  mg/L, and  $0.85 \pm 0.18$  mg/L were detected in aluminum cookware. Furthermore, the mentioned heavy metals were detected at  $2.02 \pm 0.7$  mg/L,  $0.5 \pm 0.4$  mg/L, and  $3.22 \pm 0.25$  mg/L concentrations in steel utensils (Ojezele et al. 2016).

On the other hand, others have also indicated high migration of Ni when scratched iron, aluminum, stainless steel, and Teflon utensils are used with mean values of  $30.3 \pm 0.56$  mg/L,  $21.56 \pm 0.12$  mg/L,  $28.98 \pm 0.09$  mg/L,  $14.54 \pm 0.15$  mg/L, respectively (Said 2015).

Moreover, Kuligowski et al. reported that cooking food in utensils made of stainless steel has a release potential of 0.015 mg Cr in a day into the diet of an individual; however, this can increase to more than 100 times when utensils are made of mild steel and cast iron cookware (Kuligowski and Halperin 1992).

Around 50% of the annual nickel production is applied to making stainless steel. The food handling industries extensively utilized stainless steels and other nickel-comprising compounds. Some researchers have revealed that the nature of cooking wares, cooking process, and storage procedures may increase the concentration of trace metals in food (Dan and Ebong 2013). In this regard, significant amounts of trace metals can be released into the food as a result of high cooking temperatures, acidic conditions, and container damage and corrosion, which subsequently can seriously affect the endocrine system over the years and may result in adverse health effects (Kuligowski and Halperin 1992).

Daily exposure to heavy metals via cosmetic products has also been regarded as a negligible source for individuals compared to the main sources such as food, water, and the air. However, due to the cumulative property of trace metals in the human body during the life period, cosmetics can be considered a significant source of exposure to heavy metals

**Table 2** Mean concentration of heavy metals ( $\mu\text{g/g}$  creatinine)

Creatinine-adjusted heavy metals ( $\mu\text{g/g}$ creatinine)	Recovery (%)	LOD ( $\mu\text{g/L}$ )	Min	Percentile			Max	Mean $\pm$ SD
				25th	50th	75th		
Ni	100	0.3	0.5	2.1	3.1	5	33.3	4.1 $\pm$ 3.4
Cr	100	0.15	0.17	4.5	6.7	8.9	33	7.5 $\pm$ 4.8

**Table 3** The mean concentration of urinary heavy metals (µg/g creatinine) across categories of some variables

Variables			Cr		Ni		
			Mean (SD)	p-value**	Mean (SD)	p-value**	
Education level		Academic	29.4 (10.6)	0.3	14.4 (12.8)	0.6	
		High school	7.9 (4.5)		3.9 (2.5)		
		< High school	11.6 (3.7)		5.1 (1.4)		
Family income		Low	7.7 (4.4)	<b>0.09</b>	3.8 (2.1)	<b>0.07</b>	
		Middle	7.3 (5.2)		3.6 (2.6)		
		High	7.8 (2.8)		3.8 (0.9)		
Used utensils for cooking	Zinc	No	7.6 (5.3)	0.8	3.4 (0.4)	0.9	
		Yes	7.4 (3.5)		3.8 (0.2)		
	Copper	No	6.5 (3.7)	<b>&lt;0.001</b>	3.4 (3.3)	<b>&lt;0.001</b>	
		Yes	12.6 (6.7)		6.3 (3.4)		
	Aluminum	No	6.7 (3.7)	<b>&lt;0.001</b>	3.2 (1.8)	<b>&lt;0.001</b>	
		Yes	11.7 (7.5)		7.2 (6.8)		
	Teflon	No	6.2 (3.4)	<b>&lt;0.001</b>	3.1 (1.9)	<b>0.04</b>	
		Yes	8.9 (5.7)		4.7 (4.4)		
	Enameled	No	7.3 (4.9)	<b>0.02</b>	3.9 (3.6)	0.4	
		Yes	10.9 (3.5)		4.7 (1.5)		
	Cast Iron	No	7.5 (4.1)	0.9	3.8 (2.3)	0.6	
		Yes	7.5 (6.1)		4.1 (5.1)		
	Steel	No	5.2 (2.3)	<b>&lt;0.001</b>	2.6 (1.5)	<b>&lt;0.001</b>	
		Yes	11 (5.5)		5.8 (4.5)		
	Pyrex	No	7.5 (4.9)	0.6	3.9 (3.5)	0.5	
		Yes	8.3 (3.1)		4.7 (2.9)		
	Maternal occupation		House holder	7.9 (5)	0.4	3.8 (2.3)	0.2
			Employed	30.1 (13.9)		13.8 (8.4)	
Used scratched utensils		No	6.3 (3.3)	<b>0.008</b>	3 (1.9)	<b>0.01</b>	
		Yes	8.4 (5.6)		4.6 (4)		
Cosmetic use		Yes	9.2 (5.1)	<b>&lt;0.001</b>	4.8 (3.8)	<b>&lt;0.001</b>	
		No	4.7 (2.7)		2.2 (1.3)		
Seafood consumption		Low	7.1 (4.7)	0.2	3.2 (2.3)	<b>0.001</b>	
		Moderate	7.4 (4.5)		3.7 (1.2)		
		High	9.4 (6.3)		6.9 (1.2)		
Used canned foods		Low	6.8 (4.4)	0.1	3.1 (2.2)	<b>0.001</b>	
		Moderate	8.2 (5.1)		4.1 (2.1)		
		High	9 (6.1)		6.4 (1.6)		
Passive smoking during pregnancy		Yes	8.4 (5.2)	<b>0.02</b>	4.5 (1.5)	<b>0.05</b>	
		No	6.6 (4.4)		3.3 (1.2)		
Physical activity		Low	6.4 (3.9)	<b>&lt;0.001</b>	3 (1.9)	<b>&lt;0.001</b>	
		Moderate	6.4 (3.8)		3.3 (2.4)		
		High	11.2 (6.9)		6.5 (5.4)		

Highlighted value: significant p-value <0.05

\*\*p-value found by t-test and ANOVA after normalization

(Castro-González and Méndez-Armenta 2008). This is in accordance with our results showing a significant difference between cosmetic use and the mean concentration of Cr and Ni (p-value <0.001).

Conferring to Health Canada, more than 90% of cosmetic products were positively confirmed in terms of the presence of

some important heavy metals such as Pb, Cd, Ni, As, and Hg (Orisakwe and Otaraku 2013). The mentioned heavy metals are extraordinarily toxic and their use as ingredient of cosmetic products has been prohibited in the EU and the USA (Kohli 2017). However, previously, some Iranian researchers have detected Cr, Pb, and Ni with the amounts of 2270 ± 240 ng/

g,  $61900 \pm 1900$  ng/g, and  $3380 \pm 210$  ng/g, respectively, in some cosmetic products. Though Cr, Ni, and Pb concentrations were lower than the WHO standards, they can be accumulated when used continuously (Ghaderpoori et al. 2020).

Moreover, some previous evidence also shows that pregnant women and their neonates are at higher risk of exposure to heavy metals and related complications because of cosmetic use (Li et al. 2019). Li et al. reported that cosmetic usage was correlated with an increased risk of SGA (small gestational age) in pregnant women (OR = 1.23, 95% CI) in comparison with non-consumers (Li et al. 2019).

We also observed significant variations in the urinary concentrations of Cr (p-value=0.02) and Ni (p-value=0.05) in participants who were passively exposed to smoke.

Previous studies show that Cr is found in the mainstream cigarette/smoke with an amount of 0.0002–0.5 mg per cigarette (Fadaei et al. 2021). Furthermore, about 4.3 mg/kg concentrations of Cr were detected in individuals exposed to smoke compared to non-smokers (Feng et al. 2015). Additionally, 0.64 and 1.15 mg/g Ni concentrations were measured in the tobacco plant and 0.078–5 mg/g in cigarettes (Hajizadeh et al. 2020).

Similar to our findings, Chiba et al. also detected Cd, Cr, Ni, and Pb in smoke/cigarettes and also in body fluids of individuals who were smokers. They also showed that individuals who were passively exposed to smoke can accumulate greater amounts of heavy metals (Chiba and Masironi 1992).

Several other studies have also reported that high levels of heavy metals from smoking may increase the risk of spontaneous abortion (Rzyski et al. 2015), preterm delivery, stillbirth, and smaller infant weight (Mittal 2019).

Bonferroni post hoc test for seafood consumption showed that the mean urinary Ni concentrations were significantly different from the other two categories (p-value <0.001). While, the mean concentrations of Cr and Ni were significantly higher in individuals who consumed higher amounts of canned foods (Cr: p-value=0.04 and Ni: p-value <0.001).

The majority of the food-based dietary guidelines insist on consuming more seafood during the pregnancy period to provide sufficient iodine and DHA (docosahexaenoic acid) as a key role in the development of the central nervous system of the fetus. However, serious advice is presented on the limitation of seafood consumption due to rather high heavy metal content and its vital outcome on a fetus (Tetens and Sjödin 2014).

In line with our findings, Yu et al. indicated that the rate of fish consumption during pregnancy was associated with a higher amount of heavy metals in cord blood. Females who consumed more seafood had higher levels of heavy metals in their cord blood than those who consumed less and less frequently (Yu et al. 2011).

Moreover, the study conducted in Neyshabur, Iran, demonstrated that the mean concentrations of Pb and Ni in canned

tuna samples were  $0.125 \pm 0.6$  mg/L and  $0.07 \pm 0.11$  mg/L, respectively, which were higher than the standard limit (Alidadi et al. 2019).

Our results indicated that the mean of urinary Cr and Ni concentrations at high levels of physical activity was significantly different from the other two categories (p-value <0.001). In other words, higher Cr and Ni concentrations were detected in women who had greater physical activities.

There is limited literature about the effect of physical exercise on heavy metal excretion from the tissue and body fluids. In agreement with our results, Milnerowicz et al. revealed that a greater level of physical activity is positively correlated with a higher concentration of urinary heavy metal and after 24 h it reduced lower than the initial amount. It can be supposed that with higher physical activity, a higher concentration of heavy metals permeates from blood to urine, and thus eliminated from the body. It is likely that heavy metals are additionally released from tissues to blood and urine. It can be concluded that heavy physical exercise alters heavy metal reserves in tissues. This might be considered a positive event, especially in terms of the long half-life and the range of its toxicity (Milnerowicz et al. 2004).

Physical activity increases oxygen consumption, and consequently, reactive oxygen species (ROS) production elevates. Regular and moderate physical exercise releases oxidative stress, increases cellular adaptation, and also decreases the quantity of lipid peroxidation products developing within activity performance (Gimiastis 2003; Milnerowicz et al. 2004). In this circumstance, cells in response to stress generate various proteins, including metallothionein (MT). This protein arrests heavy metals, therefore lessening their poisoning effects. Moreover, metallothionein, known as a protein of acute phase, serves as an effective free radical scavenger, therefore reducing cellular damages (Amin et al. 2019a, 2018b; Lauwerys and Bernard 1987; Milnerowicz et al. 2004).

## Strengths and limitations

To the best of our knowledge, this study is one of the first reports to examine the possible associations between lifestyle and socio-demographic characteristics among Iranian pregnant women with prenatal heavy metal exposure. However, we found some limitations in the current study which may affect the findings. The medium or small size of the samples with typically similar lifestyle and socio-demographic characteristics of participants might affect the statistical findings. However, we were able to find a significant relationship between lifestyle and socio-demographic factors with the heavy metal concentrations. In addition, in this study, we collected spot urine samples. It was not possible to prepare representative urine samples during the day (24-h urine); this may not severely affect the total distribution of heavy metals among

the studied individuals. We attempted to address this by adjusting urinary creatinine levels.

## Conclusion

This study was performed to determine the concentration of urinary heavy metals with maternal lifestyle variables and characteristics of pregnant women. According to the findings, the following conclusions can be made:

- Chromium and nickel were detected in all urine samples of the studied participants.
- The detected mean concentration of chromium and nickel had a higher value in the urine of Iranian pregnant females in comparison with other countries.
- The mean concentrations of chromium and nickel were higher in participants who were second-hand smokers; users of copper, aluminum, Teflon, steel, enameled, and also scratched utensils for cooking; and consumers of sea-food and canned foods; and individuals with higher physical activity.
- The lifestyle determinants and cosmetic product usage were significant predictors of urinary heavy metals among pregnant females than socio-demographic characteristics such as age, education level, and maternal occupation.

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**Data availability and material** The material and raw data are available upon request.

**Code availability** None.

**Author contribution** M. Moradnia and H. Movahedian Attar surveyed the studies for data extraction and inclusion, assess the study quality, and wrote the first draft of the manuscript; Z. Heidari performed the data-analysis; F. Mohammadi provided critical input for the manuscript; Roya Kelishadi did critical revision of the manuscript. All authors have contributed considerably, and all authors are in agreement with respect to the manuscript content. The authors read and confirmed the final manuscript.

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## Declarations

**Consent to participate** All participants voluntarily agree to participate in this research study.

**Consent for publication** The studied participants consented for the publication of their identifiable details.

**Competing interests** The authors declare no competing interests.

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