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Araştırma Makalesi - Research Article

Pb-Cd in Maternal Blood and Affecting Factors

Maternal Kanda Kurşun-Kadmiyum ve Etkileyen Faktörler

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ABSTRACT

The exposure to Pb-Cd during pregnancy has negative effects on both the mother and the baby. Karabuk province, which is the center of the iron and steel industry, is a region with a high risk of Pb-Cd exposure. This study was designed to determine the levels of lead and cadmium in maternal blood samples and the factors influencing them. After the ethical committee approval from Karabük Training and Research Hospital Ethical Committee, descriptive and analytical analyses were started on the blood samples collected from 100 pregnant women in their third trimester with the childbirth between 01.09.2018-01.09.2019 in Karabük Training and Research Hospital Obstetrics and Gynecology Clinic. The study, conducted in a descriptive and analytical manner, utilized a 32-question survey form prepared by the researchers and venous blood samples collected simultaneously. For the Pb-Cd analysis, a 3 ml venous blood sample was obtained from pregnant women using a sterile syringe into hemogram tubes with purple caps containing Ethylenediaminetetraacetic acid (EDTA). The collected samples were preserved in a -20°C refrigerator immediately after labeling and were kept until they were taken for analysis. Maternal blood samples were analyzed using the Atomic Absorption Spectroscopy (AAS) Graphite System method. According to the analysis results, the mean maternal blood Pb levels of pregnant women with an average age of 28.3±5.37 were found to be 0.89±0.22 µg/dl, and Cd levels were 0.26±0.07 µg/dl. Maternal blood Pb-Cd levels were compared each other according to five parameters which are socio-demographic aspect, obstetrical variables, location characteristics, dietary history, and cosmetic use. Based on these parameters any statistically significant results were obtained. However, blood lead levels were significantly different in pregnant women who smoked ($p=0.001$) and were exposed to secondhand smoke ($p<0.05$) compared to non-smokers and those not exposed to secondhand smoke. On the other hand, there was no significant difference in blood Cd levels with respect to exposure to secondhand smoke ($p>0.05$). Since exposure to Pb-Cd is not a short-term exposure, but rather long-term exposure to low concentrations in daily life, and because their half-lives are long-term. These results obtained from this study can shed light on future studies which aimed to determine the effect of long- term exposure of heavy metals on pregnant women and infants.

Keywords- Cadmium, Heavy Metal, Lead, Maternal Blood

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ÖZ

Gebelik döneminde Pb-Cd'ye maruziyet anne ve bebek üzerinde olumsuz etkiler oluşturur. Demir çelik endüstrisinin merkezi olan Karabük ili, Pb-Cd maruziyeti bakımından oldukça riskli bir bölgedir. Bu çalışma maternal kanda Pb-Cd düzeylerini ve etkileyen faktörleri belirlemek amacıyla yapılmıştır.

Etik kurul izinleri alındıktan sonra, 01.09.2018-01.09.2019 tarihleri arasında, Karabük Eğitim ve Araştırma Hastanesi Kadın Hastalıkları ve Doğum Polikliniği'ne doğum veya kontrol/izlem yapmak üzere gelen üçüncü trimesterdeki gebeler (n=100) araştırmanın örneklemini oluşturmuştur. Tanımlayıcı ve analitik tipte gerçekleştirilen çalışmanın veri toplama araçları olarak, araştırmacılar tarafından hazırlanan 32 soruluk bir anket formu ve eş zamanlı alınan venöz kan kullanılmıştır. Pb-Cd analizi için gebeden, Etilen Diamin Tetraasetik Asit (EDTA) içeren mor kapaklı hemogram tüplerine, steril enjektör aracılığıyla 3 ml'lik venöz kan örneği alınmıştır. Alınan numuneler etiketlendikten hemen sonra -20°C soğutucuda analize gidene kadar muhafaza edilmiştir. Maternal kan numuneleri, AAS (Atomik Absorbsiyon Spektroskopisi) Grafit Sistem yöntemi kullanılarak analiz edilmiştir. Analiz sonuçlarına göre, yaş ortalamaları 28,3±5,37 olan gebelerin maternal kan Pb düzeyleri ortalama 0,89±0,22 µg.dl-1, Cd düzeyleri ise 0,26±0,07 µg.dl-1 olarak bulunmuştur. Maternal kan Pb-Cd düzeyleri; gebelerin sosyo-demografik, doğurganlık özellikleri, beslenme, kozmetik kullanımı ve lokasyon değişkenleri ile karşılaştırıldığında istatistiksel olarak anlamlı bir sonuç elde edilmemiştir. Ancak sigara içen ($p=0.001$) ve sigara dumanına maruz kalan gebelerde ($p<0.05$) kan Pb düzeyleri, sigara içmeyenlere ve sigara dumanına maruz kalmayanlara oranla anlamlı farklılık göstermiştir. Diğer taraftan, kan Cd düzeyleri ile sigara dumanına maruz kalma açısından anlamlı bir farklılık bulunmamıştır ($p>0.05$). Pb-Cd'ye maruz kalma kısa süreli bir maruziyet olmadığından, günlük yaşamda düşük konsantrasyonlara uzun süreli maruz kalma ve yarı ömrü de uzun vadeli olmasından dolayı, yürütülen bu çalışmanın sonuçları özellikle ağır metallere uzun süre maruz kalan gebeler ve bebekler üzerindeki etkilerini belirlemek amacıyla yapılacak olan çalışmalara ışık tutabilir.

Anahtar Kelimeler- Ağır Metal, Kadmiyum, Kurşun, Maternal Kan

I.INTRODUCTION

Technological advancements, which play a significant role in for human beings, also generate substantial amounts of waste [1, 2]. Artificial agricultural fertilizers, chemicals, industrial waste, petroleum and its derivatives, inorganic salts, radioactivity, detergents, pesticides, waste heat, and heavy metals are some important pollutants that disrupt the ecological balance dramatically [3, 4].

It is well-known that the exposure of environmental pollution which derived from the chemical pollutants have a long-term detrimental effect on cellular development [5]. Metals that have high concentrations but can show toxic effects even at low levels are called heavy metals [6]. There are more than 60 heavy metals, including copper, cobalt, lead, mercury, chromium, cadmium, and zinc are found trace amounts in the nature. [7, 8, 9]. Heavy metals have toxic and/or carcinogenic effects in the biological organisms and accumulate their metabolism. Their intake into the body is faster, while their metabolism and elimination are slower [7, 10]. Elements found in the human body at the mg/l (ppm) or (ppb) level are defined as heavy metals and these elements are taken into the human body through air, water, food and cigarettes. Metals that are not useful for the body, that are not excreted even if they are taken in very little, and that cause toxic effects over time are called toxic metals [11].

Many biological and chemical substances in our environment such as industrial waste and environmental pollutants, addictive substances, X-ray devices, heavy metals such as copper, mercury, lead, cadmium and arsenic, pesticides and psychotropic drugs and food additives cause toxic effects in living organisms acutely or chronically, directly or indirectly [12]. According to toxicokinetics, heavy metals can be analyzed in the body through various biological materials such as nails, teeth, saliva, bones, urine, stool, whole blood (plasma, whole blood), breast milk and cord blood [13]. Inhalation, oral intake, and/or dermal exposure of heavy metals can cause acute and/or chronic poisoning. During both the intrauterine and postpartum period long-term exposure of chemical pollutants have damaging effects on the baby's physiological systems especially nervous system [14, 15].

Lead (Pb) and cadmium (Cd) are among the top 10 heavy metals according to the Agency for Toxic Substances and Disease Registry (ATSDR)'s Priority Hazardous Substances 2007 [16].

Pb which is a heavy metal found naturally in the earth's crust and has a toxic effect [17], is mainly transmitted by inhalation (gasoline, cigarettes, etc.), water, food, transplacental route during pregnancy, dust, soil, paints, skin contact, solder on food cans and cosmetic products [18-20].

Cd, which can be rapidly converted to cadmium oxide in the air and has the highest solubility in water, is a toxic heavy metal that spreads very rapidly in nature [21]. Cd is a ubiquitous heavy metal that continuously diffuses into the environment as a result of human economic activities, has negative effects on human health, has toxic effects on multiple organs and systems and is ubiquitous. It is transmitted to the human body through occupational exposure, inhalation, diet, smoking and passive smoking or drinking water [22]. Sources of Cd affecting human life are refined foods, electricity industry, water pipes, coal burning, tea, coffee, smoking, flue gases from industrial production, fertilizers used in the seed stage, shellfish, ceramics, rubber, textiles, leather industry, plastics, fruits [23-25]. Cd has become an important environmental pollutant with industrialization. Cd from emission sources passes into the air and then into water and soil. A lot of Cd accumulates in heavy traffic, highways and their surroundings, factories and industrial zones [26]. Cd is not normally found in the organism and has toxic effects for every system. It accumulates in the kidney and liver as a result of lifelong exposure. Cd is toxic to all organisms even in very small amounts. It can cause birth anomalies, genetic mutations and cancer [27, 28].

Pregnancy, in which many changes occur simultaneously, is an important turning point for women and family life [29, 30]. It is a process in which physical, hormonal, psychological and social changes are experienced in the body in order to ensure the growth and development of the fetus and to prepare the mother's body for birth and requires adaptation to these changes. Changes in the body can return to normal within the first 6-8 weeks after birth [29, 31, 32]. In the third trimester, organs mature for extrauterine life and the fetus begins to gain weight rapidly. The body takes a round appearance and subcutaneous fat tissues are seen [33]. At the end of this period, if there are no fetal, placental and maternal adverse factors, term delivery occurs [34].

Pregnant women and fetuses are potentially highly sensitive to environmental pollutants. There are some studies in the literature related to prenatal Pb exposure. In these studies different biological materials were collected such as maternal venous blood or cord blood, nails, urine, and hair at different trimesters and measuring the level of Pb in these biological materials [35, 36]. The maternal Pb exposure level changes in a correlation with the Pb level passed through the fetus. For example, during pregnancy, Pb stored in the bones can easily pass from the placenta to the fetus, called prenatal Pb exposure. Intrauterine Pb exposure during pregnancy can lead to developmental delays, behavioral disorders, and low IQ. Although a significant portion of Pb is stored in the bones, it can still pass into the placenta, fetus brain, and breast milk. The lead accumulation rate in infants is low but it increases with the age and long-term Pb exposure [14].

Chronic exposure to Cd increases the risk of liver and prostate cancer. Some of the detrimental effects of the Cd exposure include osteoporosis, tooth loss, loss of the sense of smell, and anemia [37]. Exposure to Cd during pregnancy is harmful both the mother and the fetus because the placenta cannot create a barrier against Cd [38]. Furthermore, exposure to Cd has been associated with low birth weight, a decrease in newborn length and head circumference, as well as neurobehavioral and physiological developmental disorders [39]. Blood Cd levels are 4-5 times higher in smokers compared to non-smokers [40]. A person who smokes 20 cigarettes a day is exposed to 2-4 µg Cd [41]. Cadmium causes serious damage to reproductive organs such as ovaries and testes and embryos [42]. After Cd is ingested through vapor, it accumulates entirely in the liver. Cigarette smoke is a major source of vapor exposure, with smokers having Cd levels 4-5 times higher than non-smokers [40]. One cigarette contains around 1-2 µg of Cd. Repeated cigarette exposure causes Cd to reach toxic levels [43]. Cd level in the blood indicates the accumulation of Cd absorption in the last 3-4 months [44].

It has been known that there are limited number of clinical and experimental studies related to Pb-Cd levels and its effects during maternal period. In this study our main aim is to determine the levels of Pb-Cd, which are toxic heavy metals, in maternal blood samples and try to understand their detrimental effects, both the mother and the baby and, interpret their effects on maternal and infant health, and make recommendations for taking necessary measurements to eliminate these potential risks of these two heavy metals.

II. METHODS

Karabuk University received ethical approval for this research with the decision number 4/7 from the Karabük University Non-Interventional Ethics Committee on July 4, 2018.

Population and Sample of the Research: The population of the study consisted of all pregnant women who applied to the Obstetrics and Gynecology Outpatient Clinic of Karabuk University Training and Research Hospital between 01.09.2018-01.09.2019 for delivery or control/monitoring; the sample consisted of 100 pregnant women who voluntarily agreed to participate in the study, who could understand and speak Turkish, who had been residing in Karabuk province and its districts for at least one year, who were in the third trimester of pregnancy and who were determined by random sampling method.

***Data Collection Instruments*:** In this descriptive and analytical study, a 32-question questionnaire prepared by the researchers and venous blood drawn simultaneously were used as data collection tools.

Data Collection and Evaluation Methods and Data Analysis: Data in the study were collected using a data collection form created by the researchers. In the first stage, Pregnant women in the third trimester who applied to Karabuk University Training and Research Hospital Obstetrics and Gynecology Outpatient Clinic for delivery or control/monitoring purposes were provided with information about the purpose, significance, and procedures of the research, and informed voluntary consent was obtained. The data collection form was administered to pregnant women who agreed to participate in the study through face-to-face interviews.

In the second stage of the study, pregnant women were seated to obtain a blood sample, and 3 ml of blood was drawn with a syringe from the inner elbow vein, or alternatively, from the hand if the vein was thin or deep. After removing the needle tip, the obtained blood was transferred to a hemogram tube with a purple cap containing Ethylenediaminetetraacetic acid (EDTA) to prevent coagulation and obtain whole blood/plasma. To prevent clot formation inside the tubes, the blood was mixed 5-6 times immediately after collection but not shaken. A label with the pregnant woman's identity information was attached to the sample tube. The samples were preserved in a -20°C refrigerator immediately after labeling until they were taken for analysis. Pb and Cd analyses were conducted in a specialized toxicology laboratory. When a sufficient sample size was reached, the samples were transported to the toxicology laboratory by the researcher himself, following the cold chain rules, for analysis. Measurements of the collected blood samples in the study were performed using the Perkin Elmer AAnalyst 600 Zeeman model electrothermal atomic absorption spectroscopy (Graphite Furnace Atomic Absorption Spectroscopy). In this analysis method, blood samples are diluted with matrix modifiers buffer, which contains sodium dihydrogen phosphate, nitric acid, and Triton X-100. The instrument operates in the furnace program defined for the method. The reading time for each sample is 5 minutes. Atomic absorption spectrometry (AAS) is a single-element technique that measures the concentrations of elements. The principle is based on the measurement of the decrease in light intensity due to the absorption of electromagnetic waves emitted from the radiation source by the gaseous atoms. The radiation emitted from the hollow cathode lamp specific to the element to be measured is passed through the current flame and measured by the detector. The sample to be analyzed is sent into the flame. If the relevant element is present in the sample, the emitted radiation from the lamp is absorbed, resulting in a decrease in light intensity. The amount of absorbed radiation is directly related to the change in the concentration of the element in the sample.

Data Analysis Methods: Before proceeding to significance tests, the parametric test assumptions of normal distribution were assessed using the Shapiro-Wilk test and homogeneity of variances was evaluated using the Levene's test for the obtained data [45]. In the examination of maternal blood Pb and Cd levels in terms of the obtained variables, Mann-Whitney U test was used for comparisons between two groups, and the Kruskal-Wallis test was used for comparisons involving more than two groups. Correlations between Pb and Cd levels and continuous variables were determined using Spearman Rank correlation analysis. Results were interpreted as follows: $p < 0.05$ was considered statistically significant, while $p>0.05$ was considered statistically not significant.

III. RESULTS

The findings obtained as a result of the study conducted to investigate the Pb-Cd level in the blood of the pregnant women in the third trimester of pregnancy with an age range of 17-42 years and the factors affecting it were classified and tabulated as follows;

- Findings related to the comparison of Pb levels in maternal blood with variables such as socio-demographic aspect, obstetrical variables, dietary history and cosmetic use, smoking habits, exposure to secondhand smoke and location characteristics of pregnant women (Tables 1-5),

- Findings related to the comparison of Cd levels in maternal blood with variables such as socio-demographic aspect, obstetrical variables, dietary history and cosmetic use, smoking habits, exposure to secondhand smoke and location characteristics of pregnant women (Table 6-10).

Results Obtained by Comparison of Maternal Blood Pb Levels with Socio-Demographic Aspect of Pregnant Women

In our study, it was determined that maternal blood Pb level was 0.89±0.22 $\mu g.dl^{-1}$ and a statistically significant relationship was found between Pb levels and age ($p<0.05$). However, no significant relationship was found between Pb levels and height, previous weight, and weight gain ($p>0.05$). When the Pb levels were compared with the socio-demographic characteristics of the pregnant women, no statistically significant difference was observed between the groups ($p>0.05$) (Table 1).

Table 1. Comparison of Socio-Demographic Aspect and Blood Pb Levels of Pregnants

	n	**Arith. Cover. ± SD**	**Min-Max**
Lead Level	100	0.89±0.22	0.52-1.54
Age	100	28.3±5.37	17-42

Size		100	160.4±5.72	144-172	
Weight gained		100	11.63±5.68	1-28	
Socio-demographic characteristics		**n**	**r** [1]	**p**	
Age		100	0.214	**0.032***	
Size		100	-0.056	0.578	
Weight gained		100	0.034	0.741	
		n	**Arith. Cover. ± SD**	**Rank Avg.**	**Statistical analysis**
Educational Status	Primary school	18	0.86±0.220	45.97	H[1] = 5.292 p=0.259
	Middle school	19	0.85±0.247	44.61	
	High school	27	0.95±0.236	59.04	
	University and Above	33	0.88±0.186	51.36	
	Not Literate	3	0.75±0.185	28.67	
Job	Housewife	69	0.90±0.22	51.68	H=1.370 p=0.713
	Officer	16	0.86±0.19	46.88	
	Employee	8	0.81±0.19	42.06	
	Free	7	0.89±0.29	56.79	
Spouse Education	Primary school	18	0.88±0.23	48.92	H=0.254 p=0.968
	Middle school	28	0.91±0.25	52.36	
	High school	32	0.88±0.20	50.95	
	University/School	22	0.87±0.21	48.77	
Spouse Profession	Officer	21	0.83±0.20	41.57	H=7.473 p=0.113
	Employee	28	0.85±0.21	47.63	
	Private sector	16	0.96±0.22	60.16	
	Self-employment	29	0.95±0.24	57.60	
	Unemployed	6	0.77±0.02	77.42	
Permanent Residence	Bay	10	0.94±0.27	52.95	H=0.464 p=0.793
	District	33	0.88±0.25	47.33	
	City	56	0.89±0.19	51.04	

* $p<0.05$, r [1] :correlation coefficient, H [1] :Kruskal Wallis H Test

Results Obtained by Comparing Maternal Blood Pb Levels with Obstetrical Variables of Pregnant Women

Maternal blood Pb levels were compared between pregnant women based on their obstetrical variables. It was found that the maternal blood Pb level in women who gave birth to low birth weight was 0.83±0.17 µg.dl^{-1}, while it was 0.89±0.22 µg.dl^{-1}in women who did not give birth, and this difference was not statistically significant ($p>0.05$). In all pregnant women, when maternal blood Pb levels were compared based on the history of pregnancy termination, it was determined that the average Pb level was 0.89±0.25 µg.dl^{-1} in those who had undergone curettage and 0.89±0.21 µg.dl^{-1}-1 in those who had not, and this difference was not statistically significant ($p>0.05$). When maternal blood Pb levels were examined based on the presence of pregnancy-related hypertension (HT), it was found that those with hypertension had an average Pb level of 0.90±0.09 µg.dl^{-1}, while those without had 0.89±0.22 µg.dl^{-1}, and this difference was not statistically significant. Similarly, when gestational diabetes (GD) was considered, those with GD had an average Pb level of 0.98±0.28 µg.dl^{-1}, while those without had 0.87±0.21 µg.dl^{-1}, and this difference was not statistically significant (Table 2).

Table 2. Comparison of Variables Related to obstetrical variables of Pregnants with Blood Pb Levels

Variables		**n**	**Arith. Cover. ± SD**	**Rank Avg.**	**Statistical analysis**
Did you give birth to a low-birth-weight baby?	Yes	5	0.83±0.17	46.20	z [1] =-0.340 p=0.734
	No	95	0.89±0.22	50.73	
Have you had an abortion before?	Yes	21	0.89±0.25	50.29	z = -0.038 p = 0.970
	No	79	0.89±0.21	50.56	
Do you have HT during pregnancy?	Yes	5	0.90±0.09	57.30	z = -0.538 p = 0.591
	No	95	0.89±0.22	50.14	
Have you had GD during pregnancy?	Yes	11th	0.98±0.28	60.64	z = -1.229 p = 0.219
	No	89	0.87±0.21	49.25	

* $p<0.05$, z [1] :Mann Withney U

Results Obtained by Comparison of Maternal Blood Pb Levels with Dietary History and Cosmetic Use of Pregnant Women

When the Pb levels in the pregnant women participating in the study were compared with their dietary history and cosmetic use, no statistically significant difference was found (p>0.05) (Table 3).

Table 3. Comparison of Variables Related to Dietary History and Cosmetic Use of Pregnants with Blood Pb Levels

Variables		n	Arith. Cover. ± SD	Rank Avg.	Statistical analysis
Did you dye your hair while pregnant?	Yes	12	0.93±0.19	57.46	z^1=-0.886
	No	88	0.88±0.22	49.55	p=0.376
Did you use make-up products during pregnancy?	Yes	53	0.87±0.20	49.88	z = -0.225
	No	47	0.90±0.24	51.19	p = 0.822
Have you used skin lightening cream in the last year?	Yes	15	0.89±0.17	53.13	z = -0.459
	No	84	0.89±0.23	49.44	p = 0.646
Did you use herbal medicine during pregnancy?	Yes	7	0.89±0.23	49.14	z = -0.128
	No	93	0.89±0.22	50.60	p = 0.898
Do you consume canned food during pregnancy?	Yes	23	0.95±0.28	57.76	z = -1.172
	No	77	0.87±0.20	48.64	p = 0.241
Do you consume fish and seafood during pregnancy?	Yes	87	0.27±0.89	51.52	z = -0.912
	No	13	0.26±0.83	43.65	p = 0.362
Frequency of coffee consumption?	1 per day	15	0.85±0.07	47.20	
	2 or more per day	2	0.95±0.06	52.00	
	1 per week	25	0.92±0.07	54.18	H^1=4.088
	1 per month	13	0.81±0.08	36.58	p=0.537
	1 in a few months	6	0.91±0.03	52.75	
	I don't consume	39	0.90±0.08	53.63	

* p<0.05, z^1 :Mann Withney U z statistic, H^1 :Kruskal Wallis H Test

Results of Maternal Blood Pb Levels and Smoking Habits and Exposure to Secondhand Smoke of Pregnant Women

In this study, when the Pb level in the maternal blood was compared according to the smoking habit (1.29±0.30 μg/dl^{-1}) and not smoking habit (0.88±0.16 μg/dl^{-1}), the results were found to be statistically significant (p=0.001). Furthermore, a statistically significant difference was obtained according to whether the pregnant women were in smoking environments (0.97±0.25 μg/dl^{-1}) or not (0.85±0.15 μg/dl)$^{-1}$ (p<0.05). Accordingly, it was determined that the Pb levels of pregnant women in smoking environments were higher than those in non-smoking environments and it was statistically significant (Table 4).

Table 4. Comparison of Findings Related to Smoking Habit and Exposure to Secondhand Smoke in Pregnancy with Blood Pb Levels

Variables		n	Arith. Cover. ± SD	Rank Avg.	Statistical analysis
Do you smoke?	Yes	9	1.29±0.30	86.65	z^1 = -4,156;
	No	91	0.88±0.16	46.48	**p=0.001** *
Have you been in a smoking environment?	Yes	50	0.97±0.25	56.29	z=-2,447;
	No	50	0.85±0.15	41.81	**p=0.014** *

* p<0.05, z^1 :Mann Withney U standard z statistic

Results Obtained by Comparison of Maternal Blood Pb Levels and Location Characteristics of Pregnant Women

When the Pb level in the maternal blood was compared with the location characteristics of the pregnant women and the frequency of house staining, the findings were not found to be statistically significant (p>0.05) (Table 5).

Table 5. Comparison of Pregnants' Location Characteristics and Blood Pb Levels

Variables	Lead Level				
		n	Arith. Cover. ± SD	Rank Avg.	Statistical analysis
Is your house close to the factory?	Yes	20	0.90±0.24	53.90	z^1 = -0.586

	No	80	0.88±0.22	49.65	p=0.558
Is your house close to the bus station?	Yes	22	0.84±0.20	46.27	z = -0.774
	No	78	0.90±0.22	51.69	p=0.439
Is your house near the main street?	Yes	76	0.88±0.23	49.38	z = -0.690
	No	24	0.89±0.18	54.06	p=0.490
Is your house close to the train station?	Yes	14	0.85±0.31	43.00	z = -1.043
	No	86	0.89±0.20	51.72	p=0.297
Do you often paint your house?	Yes	17	0.83±0.18	45.06	z = -0.849
	No	83	0.90±0.23	51.61	p=0.396

* p<0.05, z [1] :Mann Withney U z statistic

Results Obtained by Comparison of Maternal Blood Cd Levels with Socio-Demographic Aspect of Pregnant Women

In our study, it was determined that the maternal blood Cd level was 0.26±0.07 $\mu g/dl^{-1}$, and the relationship between Cd levels and age, height, previous weight, and weight gain was not statistically significant (p>0.05). When Cd levels were compared with the variables constituting the socio-demographic aspect of pregnant women, no statistically significant difference was found between the groups (p>0.05); however, a statistically significant difference was found between the groups constituting the "occupation" variable (p=0.021) and the "spouse's occupation" variable (p=0.034) (p<0.05). When the "occupation" subgroups were examined in detail in terms of Cd levels, a significant difference was found between civil servants and self-employed individuals (p=0.036), while no statistically significant difference was observed between the other subgroups when compared within themselves (Table 6).

Table 6. Comparison of Socio-Demographic Aspect and Blood Cd Levels of Pregnants

		n	**Arith. Cover. ± SD**	**Min-Max**	
Cadmium Level		100	0.26±0.07	0.12-0.43	
Age		100	28.3±5.37	17-42	
Size		100	160.4±5.72	144-172	
Weight gained		100	11.63±5.68	1-28	
		n	**Arith. Cover. ± SD**	**Rank Avg.**	**Statistical analysis**
Educational Status	Primary school	18	0.28±0.084	58.97	H[1] = 2.733 p=0.603
	Middle school	19	0.26±0.074	49.45	
	High school	27	0.26±0.061	49.28	
	University and Above	33	0.25±0.085	46.44	
	Not Literate	3	0.30±0.087	62.00	
Job	Housewife	69	0.27±0.08	52.67	H=9.733 **p=0.021**
	Officer	16	0.23±0.08	37.66	
	Employee	8	0.23±0.05	37.13	
	Free	7	0.32±0.05	73.71	
Spouse Education	Primary school	18	0.30±0.08	63.47	H=5.215 p=0.157
	Middle school	28	0.25±0.07	47.48	
	High school	32	0.27±0.08	50.69	
	University/School	22	0.25±0.07	43.45	
Spouse Profession	Officer	21	0.24±0.08	39.57	H=10.422 **p=0.034**
	Employee	28	0.25±0.06	45.57	
	Private sector	16	0.29±0.08	58.38	
	Self-employment	29	0.27±0.07	53.26	
	Unemployed	6	0.34±0.08	77.42	
Permanent Residence	Bay	10	0.31±0.05	68.55	H=5.75 p=0.056
	District	33	0.27±0.08	52.06	
	City	56	0.25±0.07	45.47	

* p<0.05, H [1] : Kruskal Wallis H Test

Results Obtained by Comparing Maternal Blood Cd Levels with Obstetrical Variables of Pregnant Women

No statistically significant difference was found in the results of the analysis performed according to the blood Cd level and obstetrical variables of the pregnant women who participated in the study ($p>0.05$). In addition, no statistically significant difference was found in maternal blood Cd levels according to the presence of pregnancy-related HT and GD ($p>0.05$) (Table 7).

Table 7. Comparison of Variables Related to Obstetrical Variables of Pregnants with Blood Cd Levels

Variables		n	Arith. Cover. ± SD	Rank Avg.	Statistical analysis
Did you give birth to a low-birth-weight baby?	Yes	5	0.23±0.07	38.40	z^1=-0.958;
	No	95	0.27±0.08	51.56	p=0.338
Have you had an abortion before?	Yes	21	0.25±0.07	46.50	z=-0.712;
	No	79	0.27±0.08	51.56	p=0.477
Do you have HT during pregnancy?	Yes	5	0.26±0.05	48.30	z=-0.174;
	No	95	0.26±0.08	50.62	p=0.862
Have you had GD during pregnancy?	Yes	11th	0.28±0.06	58.50	z=-0.971;
	No	89	0.26±0.08	49.51	p=0.332

$^*p<0.05$, z^1:Mann Withney U

Results Obtained by Comparison of Maternal Blood Pb Levels with Dietary History and Cosmetic Use of Pregnant Women

When the maternal blood Cd level was compared with the dietary history and cosmetic use of pregnant women in the study, no statistically significant difference was found ($p>0.05$) (Table 8).

Table 8. Comparison of Variables Related to Dietary History and Cosmetic Use of Pregnants with Blood Cd Levels

Variables		n	Arith. Cover. ± SD	Rank Avg.	Statistical analysis
Did you dye your hair while pregnant?	Yes	12	0.27±0.07	56.33	z^1=-0.744
	No	88	0.26±0.08	49.70	p=0.457
Did you use make-up products during pregnancy?	Yes	53	0.27±0.07	52.24	z = -0.636
	No	47	0.26±0.08	48.54	p=0.525
Have you used skin lightening cream in the last year?	Yes	15	0.26±0.07	47.07	z=-0.430
	No	84	0.27±0.08	50.52	p=0.667
Did you use herbal medicine during pregnancy?	Yes	7	0.25±0.08	43.93	z=-0.622
	No	93	0.27±0.07	50.99	p=0.534
Do you consume canned food during pregnancy?	Yes	23	0.28±0.08	57.76	z= -1.370
	No	77	0.26±0.08	48.33	p=0.171
Do you consume fish and seafood during pregnancy?	Yes	87	0.27±0.08	51.22	z= -0.641
	No	13	0.26±0.08	45.69	p=0.521
Coffee frequency?	1 per day	15	0.26 ±0.07	50,50	
	2 or more per day	2	0.30 ±0.06	65.25	
	1 per week	25	0.26±0.07	54.52	H^1=4.860
	1 per month	13	0.26±0.08	37.58	p=0.433
	1 in a few months	6	0.26±0.03	63.58	
	I don't consume	39	0.26±0.08	49.46	

$^*p<0.05$, z^1:Mann Withney U z statistic, H^1:Kruskal Wallis H Test

Results of Maternal Blood Cd Levels and Smoking Habits and Exposure to Secondhand Smoke of Pregnant Women

No statistically significant difference was observed between smoking habit and exposure to secondhand smoke during pregnancy and blood Cd level ($p>0.05$) (Table 9).

Table 9. Comparison of Findings Related to Smoking Habit and Exposure to Secondhand Smoke in Pregnancy with Blood Cd Levels

Variables		n	Arith. Cover. ± SD	Rank Avg.	Statistical analysis
Do you smoke?	Yes	9	0.25±0.09	43.78	z^1 = -0.730;
	No	91	0.27±0.08	51.16	p=0.466
Have you been in a smoking environment?	Yes	50	0.27±0.08	52.43	z = -0.666;
	No	50	0.26±0.08	48.57	p=0.505

$^*p<0.05$, z^1:Mann Withney U z statistic

Results Obtained by Comparison of Maternal Blood Cd Levels and Location Characteristics of Pregnant Women

There was no statistically significant difference between Cd levels and characteristics depending on the location of the pregnant women (p>0.05) (Table 10).

Table 10. Comparison of Pregnants' Location Characteristics and Blood Cd Levels

Variables		Lead Level			
		n	Arith. Cover. ± SD	Rank Avg.	Statistical analysis
Is your house close to the factory?	Yes	20	0.25±0.08	42.95	z 1 = -1.303 p=0.193
	No	80	0.27±0.08	52.39	
Is your house close to the bus station?	Yes	22	0.26±0.08	49.48	z = -0.150 p=0.881
	No	78	0.27±0.08	50.73	
Is your house near the main street?	Yes	76	0.26±0.08	47.59	z = -1.786 p=0.074
	No	24	0.28±0.06	59.71	
Is your house close to the train station?	Yes	14	0.25±0.08	45.71	z = -0.666 p=0.505
	No	86	0.27±0.08	51.28	
Do you often paint your house?	Yes	17	0.24±0.09	42.03	z = -1.323; p=0.186
	No	83	0.27±0.07	52.23	

[*] p<0.05, z [1] :Mann Withney U

IV. DISCUSSION

Chemical pollutants causing environmental pollution have a long-term impact on cellular development [5]. Pb-Cd, among these pollutants, leads to serious health problems in all living organisms [46]. Pregnant women and fetuses, in particular, are highly sensitive to environmental pollutants [35]. When Pb accumulates in the body for a long time, it passes from the mother to the placenta and fetus during pregnancy and from breast milk to the baby after birth [14, 15].

Moving from the fact that high concentrations of heavy metals adversely affect all living organisms in the ecosystem, there is limited research in Turkey on the factors influencing Pb-Cd levels, especially in pregnant women. Therefore, this study, aimed at determining Pb-Cd values, was conducted in the city of Karabuk, which is among the few cities in our country with a notable Iron and Steel Industry. In this context, the study sample consisted of pregnant women in the third trimester who visited the Obstetrics and Gynecology Clinic of Karabuk Training and Research Hospital for childbirth and follow-up.

In our study, it was determined that the average Pb level in maternal venous blood is 0.89±0.22 µg/dl^{-1}, and the average Cd level is 0.26±0.07 µg/dl^{-1}. In a study conducted by Oktem (2018) in Karabuk, the average maternal venous blood Pb level was found to be 1.97±0.74 µg/dl^{-1}, and the Cd level was 0.73±0.24 µg/dl^{-1} [47]. Durska (2001) reported maternal venous blood Pb-Cd levels as 2.75 µg/dl and 0.09 µg/dl, respectively [48]. In a study by Iwai-Shimada et al. (2019) aiming to determine the prenatal Pb-Cd exposure level, they found that the maternal blood Pb level was 8.65-13.5 µg/dl^{-1}, and the Cd level was 0.74-1.79 µg/dl^{-1} [49]. While studies conducted in different regions observe similar and high Pb-Cd levels, the values in our study were found to be lower. These results, contrary to the reported Pb-Cd levels in pregnant women, suggest that factors affecting the accumulation of these heavy metals in the bodies of pregnant women living in the industrial city of Karabuk may be different.

In our study, Pb levels showed variations concerning certain socio-demographic aspect among pregnant women, while for some variables, no significant differences were observed (Table 1). When examining the maternal blood Pb levels in terms of demographic characteristics of pregnant women, a statistically significant relationship was found between Pb levels and age (p=0.032). Nakayama et al. (2019), in a study conducted in Japan to determine maternal blood Pb-Cd levels and determinants, concluded that the main determinants of Pb levels were the mother's age and whether she consumed alcoholic beverages [50]. In our study, it was determined that blood Pb levels varied on average between 0.75-0.95 µg/dl^{-1} according to the educational level. This result is parallel to the findings of Durska (2001) [48]. In Oktem's (2018) study, the average Pb level was found to be between 1.87-2.23 µg/dl^{-1} according to educational level [47]. Blood Pb levels in our study varied between 0.81-0.90 µg/dl based on the occupations of pregnant women, between 0.87-0.91 µg/dl^{-1} based on the educational level of spouses, and between 0.77-0.96 µg/dl^{-1} based on the occupation of spouses. No significant difference was observed in Pb-Cd levels in the blood concerning education and occupation, and this result was found to be parallel to the results of Oktem (2018) [47]. Considering that 69% of the participating pregnant women were homemakers, 16% were civil servants, 8% were workers, and 7% had worker status, it can be said that whether they were working or not, the pregnant women in the study had low Pb exposure.

In our study, no significant difference was found in the Pb levels of pregnant women according to obstetrical variables (Table 2). Accordingly, the average Pb level of mothers who gave birth to low-birth-weight babies and those who did not was determined to be between 0.83-0.89 $\mu g/dl^{-1}$. The average Pb level of those who had undergone curettage previously was found to be 0.89 $\mu g/dl^{-1}$. Motawei et al. (2012), in their study aiming to determine whether the blood Pb level in preeclamptic pregnant women exceeded normal limits, found a significant association between preeclampsia and high Pb levels in the blood [51]. Yazbeck et al. (2009), in their study, found the Pb level to be significantly higher in cases of pregnancy-induced hypertension (2.2±1.4 $\mu g/dl^{-1}$) compared to normotensive patients (1.9±1.2 $\mu g/dl^{-1}$; p=0.02) [52]. However, in our study, no significant difference was observed in the blood Pb levels between pregnant women with and without hypertension. The average Pb levels of pregnant women with and without hypertension ranged between 0.89-0.90 $\mu g/dl^{-1}$. Additionally, the average Pb levels of pregnant women with and without gestational diabetes mellitus (GDM) were determined to be 0.87-0.98 $\mu g/dl^{-1}$. Soomro et al. (2018) found a long-term environmental exposure to Pb-Cd to be associated with GDM in their studies [53]. It can be stated that the presence or absence of GDM and hypertension did not affect the Pb-Cd levels in the pregnant women participating in our study. Furthermore, women diagnosed with pregnancy-induced hypertension had Cd values of 0.26 µg/dl, and those with or without GDM had Cd values ranging from 0.26-0.28 $\mu g/dl^{-1}$. Oguri et al. (2019), in their study in Japan to determine the relationship between maternal blood Pb-Cd concentrations and GDM, concluded that Pb-Cd concentrations were slightly higher in women with GDM compared to those without GDM, but these differences were not statistically significant [54].

In a study conducted by Al-Jawadi et al. (2009), they found that coffee consumption is an important determinant for Pb levels [55]. However, in our study, no significant difference in blood Pb levels (0.81-0.95 $\mu g/dl^{-1}$) was observed based on the frequency of coffee consumption during pregnancy (Table 3).

In our study, a significant difference was found in Pb levels between pregnant women who smoked and those who did not, with higher Pb levels observed in pregnant women who smoked. Additionally, it was determined that Pb levels showed significant differences based on the exposure of pregnant women to secondhand smoke ($p<0.05$) (Table 4). Menai et al. (2012) also found a significant difference in Pb levels between pregnant women who smoked and those who did not during the pregnancy period ($p<0.05$) [56]. Therefore, pregnant women exposed to secondhand smoke had higher Pb levels.

In Oktem's study (2018), the blood Pb level was found to be 1.81-2.29 $\mu g/dl^{-1}$ according to the continuous residence, while in our study, this value was determined to be 0.88-0.94 $\mu g/dl^{-1}$ [47]. However, Falcon et al. (2002) and Röllin et al. (2009), in their studies, demonstrated that the blood Pb levels of individuals living in urban and rural areas significantly differed, with women living in urban areas having higher blood Pb levels [57, 58]. The pregnant women participating in our study were found to generally reside in locations far from the Iron and Steel factory and areas with heavy traffic. Therefore, it was considered that the similar blood Pb levels according to the residence might be related to this fact. When examining Pb levels in terms of location characteristics in our study, the average Pb values were found to be 0.88-0.90 µg/dl concerning the proximity of the house to the Iron-Steel factory, 0.88-0.90 $\mu g/dl^{-1}$ concerning the proximity of the house to the bus station, and averages ranging from 0.88-0.89 $\mu g/dl^{-1}$ concerning the proximity of the house to the main street. It was determined that the Pb levels of pregnant women did not show a significant difference according to these location characteristics (Table 5). Durska (2001) also found in her study that the Pb level was not related to the location of the house [48]. In contrast to these studies, Kim et al. (2019), in their study to determine the impact of an electronic waste recycling factory in the Guiyu town in southeast China on heavy metal concentration in pregnant women, found that the geometric mean of maternal blood Pb concentration in Guiyu was 1.74 times higher than that of women in Haojiang. This study concluded that living in the area where the electronic waste recycling factory is located poses a higher risk of exposure to heavy metals [59].

In our study, while Cd levels of pregnant women showed differences in some variables concerning their socio-demographic aspect, they did not show differences in some other variables. When examining the average Cd levels of variables that did not show significant differences, it was determined that they ranged between 0.25-0.30 $\mu g/dl^{-1}$ for education level, 0.25-0.30 $\mu g/dl^{-1}$ for spouse's education level, and 0.25-0.31 $\mu g/dl^{-1}$ for residence (Table 6). While no significant difference was observed in blood Cd levels based on education level in our study, significant differences were observed in terms of occupation (p=0.036) and spouse's occupation (p=0.034). Accordingly, it was found that the Cd level of pregnant women who were self-employed (0.32±0.05 $\mu g/dl^{-1}$) was higher than those who were civil servants (0.23±0.08 $\mu g/dl^{-1}$). When examined in terms of spouse's occupation, it was determined that the Cd levels of pregnant women whose spouses were unemployed (0.34±0.08 $\mu g/dl^{-1}$) were higher than those whose spouses were civil servants (0.24±0.08 $\mu g/dl^{-1}$).

In our study, no significant difference was observed in blood Cd levels based on the obstetrical variables of pregnant women (Table 7). In this context, it was found that the average Cd values ranged between 0.23±0.27 µg/dl^{-1} based on the condition of giving birth to low-birth-weight babies. This result is consistent with the findings of Zhang et al. (2004). Indeed, the study found no significant relationship between Cd levels and birth weight [59]. Sun et al. (2014) reported that Cd exposure significantly affected newborn birth weight [61], and Huang et al. (2017) determined a significant relationship between high maternal urinary Cd and low birth weight [62]. In Zhang et al.'s (2004) study, it was observed that Cd levels ranged between 0.25-0.27 µg/dl^{-1} based on the previous history of curettage among pregnant women [60]. In Durska's (2001) study, although there was a significant difference in Cd levels between women who had previously undergone curettage and those who had not, women who had undergone curettage had higher Cd levels [48]. Omeljaniuk et al. (2018) found that in women who had a miscarriage, blood Pb level was 35.54±11.0 µg/l, Cd level was 2.73±2.07 µg/l, while in the control group (35 women in the first trimester of pregnancy and after delivery), Pb was 27.11 ± 4.6 µg/l, and Cd was 1.035±0.59 µg/l. When compared, blood Pb-Cd levels were found to be higher in women who had a miscarriage and it was concluded that smoking habits significantly influenced this situation [63].

In our study, it was found that blood Cd levels ranged between 0.26-0.30 µg/dl^{-1} based on the frequency of coffee consumption during pregnancy (Table 8). In a study conducted by Osorio-Yáñez et al. (2018), urinary Cd was found to be negatively associated with coffee consumption [64].

When looking at the Cd levels based on the exposure to secondhand smoke during pregnancy, it was found that the Cd level was between 0.25-0.27 µg/dl^{-1} for the smoking habits and between 0.26-0.27 µg/dl^{-1} for being in a smoking environment (Table 9). However, Menai et al. (2012) found that pregnant women who smoked had higher Cd levels, and this was associated with low birth weight [56]. Higher Cd levels in pregnant women who smoke have also been observed in other studies [14, 65, 66]. Zhu et al. (2018), in their study aiming to determine the relationship between chronic exposure to secondhand smoke and toxic metal accumulation in hair in pregnant women, concluded that long-term passive smoking could potentially increase Pb-Cd levels [67].

When examining Cd levels in terms of location characteristics, it was found that the average Cd values ranged between 0.25-0.27 µg/dl^{-1} based on the proximity of the house to the Iron-Steel factory, between 0.26-0.27 µg/dl^{-1} based on the proximity of the house to the bus station, and the averages ranged between 0.26-0.28 µg/dl^{-1} based on the proximity of the house to the main street. Cd levels of pregnant women participating in the study did not show a significant difference based on the location characteristics (Table 10). This result is consistent with the findings of Durska (2001) [48]. However, according to the research conducted by Tavakkali and Khanjani (2016), high exposure to Cd was found in industrial workers and those with environmental exposure due to living in industrial areas [68], which contradicts the results of our study.

V. RESEARCH AND PUBLICATION ETHICS

In the study conducted on maternal blood Pb and Cd levels and the factors affecting them, the ethical principles and guidelines for research and publication were meticulously followed. The following ethical considerations were taken into account during the planning, implementation, and reporting phases of the research:

Institutional Ethical Approval: The study obtained ethical approval from the non-ınterventional ethics committee of Karabuk University (Approval Number: 4/7, Date: 04.07.2018).

Informed Consent: Informed consent was obtained from all participants. The purpose of the study, data collection procedures, and the potential risks and benefits were explained to each participant, and their written consent was obtained.

Confidentiality: The privacy and confidentiality of the participants were strictly maintained. Personal information was anonymized, and the data was stored securely to prevent unauthorized access.

Data Collection Tools: The data collection tools were developed based on a comprehensive literature review and were designed to respect the rights and privacy of the participants.

Data Collection Procedure: Data collection was carried out with the utmost care and consideration for the well-being of the participants. Blood samples were collected using appropriate medical procedures.

Data Analysis and Reporting: The data analysis was conducted rigorously and transparently, following standard statistical methods. The results were reported accurately and without bias.

Authorship and Acknowledgments: Authorship was determined in accordance with the contributions of individuals to the research. All contributors were appropriately acknowledged in the publication.

Plagiarism and Citations: Plagiarism was strictly avoided in the research, and all sources of information and previous studies were properly cited and referenced.

Publication Ethic: The research adheres to the principles of responsible and ethical publication. It was not simultaneously submitted to multiple journals, and the publication guidelines of the selected journal were followed.

Conflict of Interest: Any potential conflict of interest was disclosed, and the research was conducted impartially and without bias.

Overall, the research followed ethical standards and guidelines to ensure the integrity, credibility, and reliability of the study findings and the responsible dissemination of research results.

VI. CONCLUSION

The exposure to Pb-Cd during pregnancy has negative effects on both the mother and the baby. Karabuk province, which is the center of the iron and steel industry, is a region with a high risk of Pb-Cd exposure. This study aims to determine the levels of Pb-Cd in maternal blood and the factors influencing them. According to the analysis results, the mean maternal blood Pb levels of pregnant women with an average age of 28.3±5.37 were found to be 0.89±0.22 µg/dl, and Cd levels were 0.26±0.07 µg/dl. When maternal blood Pb-Cd levels were compared with the socio-demographic aspect, obstetrical variables, dietary history, cosmetic use and location characteristics of pregnant women, no statistically significant results were obtained. However, in smokers and pregnant women exposed to secondhand smoke, blood Pb levels showed significant differences compared to non-smokers and those not exposed to secondhand smoke. On the other hand, no significant difference was found in blood Cd levels concerning exposure to secondhand smoke.

According to the results of this study, smoking, either actively or passively, has been indicated as a significant factor in maternal blood Pb-Cd levels. Women planning for pregnancy and pregnant women should be educated, made aware of the short and long-term adverse effects of smoking, and smoking habits should be controlled. There is existing evidence in the literature regarding the negative effects of heavy metal exposure on pregnant women and fetuses. The relatively low metal-loaded air pollution due to the distance from the factory and the majority of participating pregnant women being away from the factory, bus station, and train station may have contributed to the lower metal burden in maternal blood in our study. More comprehensive studies are needed to better investigate the factors contributing to Pb-Cd toxicity.

Although Pb-Cd levels were not found to be high in pregnant women residing in Karabuk province, the findings obtained in the scope of this research will contribute to the literature with a more extensive sample size upon replication.

RECOMMENDATIONS

-To inform women of reproductive age and pregnant individuals about the risks associated with heavy metal exposure, particularly Pb-Cd, public awareness campaigns should be organized.

-Increased awareness should be emphasized on the adverse effects of smoking, both active and passive, during pregnancy, on maternal blood Pb-Cd levels. The importance of avoiding such exposures during pregnancy should be highlighted.

-By integrating preconception counseling services into routine healthcare practices, women should be provided with information about the potential risks of heavy metal exposure, and lifestyle changes should be encouraged before conception.

-Routine monitoring programs should be established, especially in industrial areas or regions with potential environmental pollution, to assess heavy metal levels in pregnant women.

-Maternal blood Pb-Cd levels should be regularly checked during prenatal care visits, and interventions should be promptly implemented upon identifying potential risks.

-Encouraging additional research with larger sample sizes is essential to comprehensively investigate factors contributing to Pb-Cd toxicity in pregnant women.

-Longitudinal studies should be conducted to examine the long-term effects of heavy metal exposure on both maternal and fetal health.

-Efforts should be made to develop and implement policies aimed at reducing heavy metal exposure in the general population, with a specific focus on vulnerable groups such as pregnant women.

-Collaboration between health authorities and industries should be promoted to develop strategies for minimizing environmental impacts of industrial activities, reducing heavy metal emissions, and ensuring environmental safety.

-Research findings should be shared with healthcare professionals and integrated into clinical practice to enable informed decision-making and personalized care for pregnant individuals.

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