Trace element biomonitoring in hair and blood of occupationally unexposed population residing in polluted areas of East Kazakhstan and Pavlodar regions

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ABSTRACT

Introduction: Eastern and North-Eastern regions of Kazakhstan are considered to be environmentally disadvantaged due to industrial pollution and activity of the former Semipalatinsk Nuclear Test Site. Ferrous metallurgy is represented by the world's largest ferroalloy plant located in Aksu. In addition to a ferroalloy plant, Aksu is the home for the largest thermal power plant in Kazakhstan.
Objective: Biomonitoring of 31 hair and blood trace elements (Ag, Ba, Be, Bi, Cs, Co, Ce, Cr, Cu, Eu, Gd, Hf, In, La, Li, Mn, Mo, Nb, Nd, Pb, Sc, Sn, Tl, Th, U, V, W, Y, Yb, Zn, and Zr) in non-occupationally exposed population residing in polluted areas of East Kazakhstan and Pavlodar regions.
Methods: Five case groups, residing in the vicinity to the former Semipalatinsk Nuclear Test Site (Akzhar, Borodulikha, and Karaul) or in proximity to industrial plants (Aksu and Ust-Kamenogorsk) have been assessed vs. controls from a rural settlement in Kurchum. In total, 204 hair and blood samples were analyzed by inductively coupled plasma mass spectrometry.
Results: The observed blood concentrations of trace elements were in agreement with earlier studies on residents of industrially polluted areas. Elevated levels of blood Ba, Mn, Pb, V, and Zn were detected in residents of Aksu and Ust-Kamenogorsk. The elemental composition of head hair was characterized by greater stability between the study sites.
Conclusion: Residency near the former Semipalatinsk Test Site could be considered as safe, while the environmental status of industrial settlements appears to be rather adverse.

1. Introduction

Modern Kazakhstan is an industrial state with abundant natural resources, which are presented both by minerals and raw materials. The country is the leading world uranium producer with the second largest uranium deposits [1]. Also, it was estimated that Kazakhstan possesses the second biggest deposits of lead, zinc and chromium and the third biggest deposits of manganese. Besides, Kazakhstan ranks in the top five for copper and in the top ten for gold and iron. As for oil and natural gas, Kazakhstan has the 11th biggest explored deposits, which are mostly concentrated on the Caspian shore. Overall, 99 chemical elements have been explored in the subsoil of Kazakhstan [2].

Pavlodar and East Kazakhstan regions are two outposts of Kazakhstan's ore mining and processing industry, being the parts of a large diversified industrial complex. Ferrous metallurgy is represented by the world's largest ferroalloy plant located in Aksu – a town in Pavlodar region. It produces ferrochromium, ferrosilicon, ferrosilico-manganese, and ferrosilicon chromium. In addition to a ferroalloy plant, Aksu is the home for the largest thermal power plant in Kazakhstan [3]. Ust-Kamenogorsk – a capital city of East Kazakhstan region, is the center of nonferrous metallurgy. The bulk of metallurgical complex of Ust-Kamenogorsk is composed of zinc refinery, lead smelter, copper plant, precious metals refinery, and acid plant.

Furthermore, the city has a titanium and magnesium plant and processes beryllium, tantalum, uranium, and niobium. Polymetal ores are mined near the city [4]. High industrial activity results in increased metal emissions into the environment [5,6], predisposing local populations to metal exposure [7].

The unfavorable environmental situation in East Kazakhstan and Pavlodar regions is also coupled with the former activity of Semipalatinsk Nuclear Test Site (SNTS), the largest ground for testing nuclear weapons in the Soviet Union [8]. Overall, 456 nuclear tests were carried out from 1949 to 1989, of which 30 were on the ground, 86 were on the air, and 340 were underground [9]. However, only a few tests contributed to significant radio-contamination of the surrounding areas, and the fallout went as far as nearby regions of the Russian Federation [10]. Health effects associated with exposure of Kazakhstani population to radiation from the SNTS have been extensively studied [11,12]. Although a number of studies have assessed radionuclide exposure in Semipalatinsk and other regions [13], the existing data on heavy metal exposure are insufficient. However, an earlier study in former U sites in Tajikistan also revealed significant environmental contamination with heavy metals [14].

Biomonitoring of trace elements is an internationally recognized tool utilized for the assessment of environmental safety [15]. As different contaminants have different routes of exposure, a number of biological samples could be used for biomonitoring, including urine [16], blood [17], serum and blood plasma [18], saliva [19], nails [20] and hair [21]. All listed biological substrates have both advantages and disadvantages. Particularly, nails and hair grow slowly and accumulate pollutants over a long period, but they are inhomogeneous and carry a high probability of external contamination. As for blood and urine, most metals tend to disappear quickly from general flow following intake, making these media unsuitable for biomonitoring in certain cases [22]. In general, the level of trace elements in blood and urine is mostly used as an indicator of acute overexposure [23]. Therefore, simultaneous analysis of certain biological samples is considered to be beneficial in biomonitoring studies that may help to overcome the potential limitations for certain substrates.

Generally, the existing data demonstrate that populations living in the Pavlodar region, as well as in proximity to SNTS face a high risk of metal overexposure, although the existing data from human biomonitoring are insufficient. Therefore, the objective of the study was the assessment of 31 trace elements (including rare earth) in blood and hair of people living in the vicinity of the Semipalatinsk Nuclear Test Site or in environmentally disadvantaged areas of East Kazakhstan and Pavlodar regions in comparison with the population of the ecologically safe zone.

2. Materials and methods

2.1. Characteristics of study sites, study subjects, and study procedures

The study followed the ethical guidelines depicted in the Declaration of Helsinki 1964 with later amendments. All study participants gave written consent before inclusion and were informed about the study aim, study procedures, and expected outcomes. Confidential treatment of personal data was also guaranteed. The study was approved by the Ethics Committee of Semey Medical University (Protocol No 6, April 27th, 2017). All investigators received training sessions before the study beginning, which covered the study aim, study procedures, and taking samples of biological media.

The overall number of study participants was equal to 204 people aged 18–50 years permanently residing at the territories of East Kazakhstan and Pavlodar regions of Kazakhstan Republic. The exclusion criteria were: (1) presence of any acute or chronic severe somatic pathology, (2) reported history of viral hepatitis B or C, (3) presence of metallic implants, (4) current dieting or consumption of multivitamin/mineral supplements, (5) chemically dyed hair, (6) pregnancy or lactation, and (7) occupational exposure to heavy metals. The duration of residence at the study sites was ascertained through automated state medical registry (ASMR) and only permanent residents were included. ASMR is a major database designed to collect data on individuals affected by the SNTS and information about available data along with its application for epidemiological studies has been presented earlier [24–26].

One hundred and twenty-eight participants were enrolled from East Kazakhstan region, and 76 participants were enrolled from Pavlodar region. Out of those enrolled from East Kazakhstan, 53 subjects lived in Ust-Kamenogorsk city, 25 subjects lived in Borodulikha village of Borodulikha district, 25 subjects lived in Karaul village of Abayskiy district, and 25 subjects lived in Kurchum village of Kurchum district. As for Pavlodar region, 50 subjects were enrolled from Aksu town, and 26 subjects were enrolled from Akzhar village. The rationale behind the selection of such study sites is that Ust-Kamonogorsk and Aksu are two urban industrial centers known for possible environmental contamination, while Borodulikha, Akzhar, and Karaul are villages located at the proximity to the SNTS. Kurchum village was selected as a control site for its known environmental safety. In the present study, the minimal distance between the case and the control setting is about 210 km (Fig. 1).

2.2. Samples of biological media

Samples of scalp hair were collected from frontal, temporal, occipital, and parietal areas in a quantity of 0.2-0.3 g. All study participants were asked to wash their hair before sampling with their ordinary shampoos. Hair was cut with precleaned scissors made of stainless steel as close to the skin as possible. Immediately after collection, the hair samples were packed into precleaned hermetic polyethylene bags labeled with identifying the number and subsequently sent to the laboratory for subsequent treatment. Special precautions were taken at all stages of sample handling to avoid external contamination.

Before elemental analysis, the hair samples were subjected to the standardized cleaning procedure, starting with washing in acetone for 10 min. Afterward, the hair samples were rinsed with deionized water three times and dried at 60 °C to constant weight. At the next step, 100 mg of hair samples were placed into Teflon tubes with concentrated nitric acid and subjected to microwave-assisted digestion for 20 min at 170–180 °C in Berghof Speedwave 4 system. After the system was cooled, distilled deionized water was added to the obtained solution up to a total volume of 15 ml, and the resulting solution was used for elemental analysis.

Blood samples were collected in the morning after night fasting from a cubital vein using vacuum test-tubes (Vacutest®) with lithium heparin as an anticoagulant. Collected blood samples were frozen at -20 °C and transported to the laboratory, where blood was thawed at +4 °C. The collected blood samples were placed into Teflon tubes with concentrated nitric acid for subsequent digestion.

The levels of silver (^{107}Ag), barium (^{135}Ba), beryllium (^{9}Be), bismuth (^{209}Bi), cesium (^{133}Cs), cobalt (^{59}Co), cerium (^{140}Ce), chromium (^{53}Cr), copper (^{63}Cu), europium (^{153}Eu), gadolinium (^{157}Gd), hafnium (^{178}Hf), indium (^{115}In), lanthanum (^{139}La), lithium (^{7}Li), manganese (^{55}Mn), molybdenum (^{95}Mo), niobium (^{93}Nb), neodymium (^{146}Nd),

Fig. 1. Map of Kazakhstan showing East Kazakhstan and Pavlodar regions with the Semipalatinsk Nuclear Test Site (SNTS) (A) and location of study sites (B).

lead (^{207}Pb), scandium (^{45}Sc), tin (^{118}Sn), thallium (^{205}Tl), thorium (^{232}Th), uranium (^{238}U), vanadium (^{51}V), tungsten (^{184}W), yttrium (^{89}Y), ytterbium (^{182}Yb), zinc (^{66}Zn), and zirconium (^{90}Zr) were analyzed using inductively coupled plasma mass spectrometry (ICP-MS) with iCAP Q (Thermo Fisher Scientific Inc., Bremen, Germany) equipped with CETAC ASX-520 auto-sampler (CETAC Technologies, Omaha, NE, USA). The system was prepared and calibrated in accordance with the manufacturer's operating manual, and tuning was performed daily using the auto-tune parameters. The following analytical parameters were used: RF power 1550 W; Argon Gas: Nebulizer flow – 1.08 L/min, Auxilliary flow – 0.80 L/min; Cool flow – 14.00 L/min; Spray chamber: Quartz cyclonic spray chamber; Sensitivity: Li^7 – 81 935CPS CPS, Co^{59} – 104 000 CPS, In^{115} – 227 156 CPS, U^{238} – 350 536 CPS; Background 4.5 – 0.65 CPS, 220.7 – 0.07 CPS; Average oxides (CeO$^+$/Ce$^+$) 0.0161, Ba^{++}/Ba 0.0203. All measurements were taken in triplicate. The multi-element standard solutions were used and the limits of quantification for blood/hair samples were: Ag (0.0006), Ba (0.002), Be (0.0001), Bi (0.0002), Cs (0.0001), Co (0.001), Ce (0.0003), Cr (0.01), Cu (0.02), Eu (0.00003), Gd (0.00006), Hf (0.0008), In (0.0001), La (0.0002), Li (0.005), Mn (0.02), Mo (0.003), Nb (0.002), Nd (0.0002), Pb (0.03), Sc (0.07), Sn (0.001), Tl (0.00,002), Th (0.0002), U (0.00003), V (0.01), W (0.0005), Y (0.0004), Yb (0.00004), Zn (0.02), Zr (0.001) (µg/L each). A randomized manner was applied for all samples to reduce possible uncertainty from the artifacts caused by instrumental sensitivity change and injection order.

2.3. Statistical data analysis

All statistical tests were performed with the help of IBM SPSS Statistics 20 for Windows software. At the first step, the Shapiro-Wilk test was used to assess the normality of data. As the data distribution was not proven to be normal, the descriptive statistics were generated by computing the median and the respective 25 and 75 percentile boundaries. Kruskal—Wallis test was used for group comparisons. The significance level of all statistical tests was present at $p < 0.05$.

3. Results

Table 1 presents demographic data of the study subjects depending on the place of residence. Women represented the major part of the population studied (74%) with very little variation between different study sites. Also, the age distribution was equivalent between all sites covered by this study. The median age ranged from 32 years for residents of Karaul village to 39 years for residents of Akzhar village and

Table 1
Demographic characteristics of the studied population.

Place of residence	Number	Gender				Median age (25; 75)
		Male Number %		Female Number %		
Kurchum	25	7	28.0	18	72.0	34 (26; 39)
Ust-Kamenogorsk	53	14	26.4	39	73.6	34 (29; 43)
Akzhar	26	6	23.1	20	76.9	39 (32; 44.5)
Aksu	50	13	26.0	37	74.0	39 (29; 48)
Borodulikha	25	6	24.0	19	76.0	37 (29; 46)
Karaul	25	7	28.0	18	72.0	32 (25; 40)
Total	204	53	26.0	151	74.0	35 (29; 45)

Aksu town.

The trace element content of hair was relatively stable between the study sites both in case of essential and toxic trace elements (Table 2). In particular, the contents of Be, Bi, Co, Eu, Gd, Hf, In, Tl, Th, U, and Yb were very low (< LOD) and did not differ between residents of Kurchum, Ust-Kamenogorsk, Karaul, Borodulikha, Akzhar, and Aksu. The residents of Borodulika had 13% higher levels of hair Pb and 17% higher levels of hair Sn as compared to residents of control Kurchum village, which was significant. Moreover, Sn levels in residents of Akzhar and Ust-Kamenogorsk were 26 and 21% higher than those in the control group, respectively. At the same time, hair Sc level in residents of Akzhar village was 18% higher than that in the control group. Besides, hair Ag levels in residents of Ust-Kamenogorsk and Borodulikha were 15 and 16% higher than those in the control group, respectively. No significant difference in hair Cs levels was detected between the study sites, except for Aksu. However, the control group was characterized by the highest hair level of Ba, significantly exceeding that of Ust-Kamenogorsk by 46%. Hair Ce levels in residents of the control site were 8, 30, and 38% higher than those in residents of Aksu, Ust-Kamenogorsk, and Akzhar, respectively, and this difference was significant.

As for the observed changes of essential trace element content, the highest levels of hair Cr were detected in residents of Akzhar, Ust-Kamenogorsk, and Borodulikha, while the lowest was observed in residents of control site and Karaul. Likewise, the hair levels of Cu in the control group were 20, 14, and 11% lower than those in Ust-Kamenogorsk, Akzhar, and Aksu, respectively. The highest hair Mn levels were detected in residents of control site, significantly exceeding those in residents of all other study sites. There was no significant difference in hair Mo levels between the study sites, except for Aksu,

Table 2
Hair trace element content (µg/L) in environmentally exposed and non-exposed persons.

Element	Control (Kurchum)	Ust-Kamenogorsk	Akzhar	Aksu	Borodulikha	Karaul
[07]Ag	0.08 (0.076-0.087)	0.092* (0.085-0.098)	0.0835 (0.075-0.099)	0.0905* (0.084-0.101)	0.093* (0.084-0.102)	0.08 (0.071-0.088)
[135]Ba	1.448 (1.22-1.585)	0.992* (0.889-1.085)	0.93* (0.829-1.079)	1.012* (0.974-1.102)	1.072* (1.008-1.13)	1.27* (1.183-1.303)
[140]Ce	0.073 (0.065-0.081)	0.056*(0.046-0.068)	0.053* (0.045-0.063)	0.0675* (0.056-0.074)	0.074 (0.065-0.081)	0.072 (0.063-0.08)
[133]Cs	0.069 (0.062-0.076)	0.065 (0.059-0.071)	0.0655 (0.052-0.073)	0.0625* (0.057-0.07)	0.064 (0.059-0.073)	0.064 (0.058-0.073)
[53]Cr	0.273 (0.249-0.307)	0.298* (0.271-0.334)	0.302* (0.26-0.323)	0.287 (0.268-0.319)	0.296 (0.267-0.321)	0.273 (0.241-0.294)
[63]Cu	13.5 (12.621-14.741)	16.264* (15.218-17.263)	15.365* (14.316-16.675)	15.01* (13.61-16.073)	15.146 (13.48-16.45)	14.04 (12.84-14.725)
[139]La	0.037 (0.032-0.04)	0* (0-0)	0.021* (0.017-0.027)	0.0265* (0.022-0.029)	0* (0-0.023)	0* (0-0)
[7]Li	0 (0-0.059)	0.071* (0.062-0.077)	0.0705* (0.059-0.081)	0.0765* (0.072-0.08)	0.076* (0.069-0.083)	0.058* (0-0.069)
[55]Mn	1.259 (1.194-1.302)	1.161* (1.148-1.166)	1.159* (1.144-1.176)	1.1485* (1.135-1.163)	1.19* (1.181-1.207)	1.214* (1.154-1.267)
[95]Mo	0.067 (0.06-0.073)	0.066 (0.058-0.073)	0.0565 (0.05-0.09)	0.073* (0.064-0.09)	0.067 (0.057-0.075)	0.067 (0.06-0.072)
[146]Nd	0.016 (0.013-0.018)	0.019* (0.016-0.021)	0.016 (0.014-0.02)	0.016 (0.014-0.018)	0.016 (0.014-0.018)	0.017 (0.014-0.019)
[207]Pb	0.942 (0.833-1.025)	0.93 (0.859-0.989)	0.9105 (0.831-0.993)	0.891 (0.829-1.012)	1.061* (0.964-1.145)	0.934 (0.822-1.013)
[45]Sc	0.186 (0.182-0.198)	0.196 (0.163-0.227)	0.22* (0.201-0.244)	0.191* (0.168-0.211)	0.198 (0.183-0.214)	0.17 (0.161-0.181)
[118]Sn	0.17 (0.161-0.175)	0.205* (0.189-0.224)	0.214* (0.189-0.232)	0.196* (0.185-0.213)	0.199* (0.188-0.219)	0.168 (0.159-0.174)
[51]V	0.154 (0.145-0.167)	0.141* (0.131-0.156)	0.1335* (0.122-0.145)	0.1375* (0.121-0.152)	0.17* (0.145-0.193)	0.152 (0.146-0.163)
[184]W	0.071 (0.068-0.08)	0.08 (0.071-0.084)	0.066* (0.048-0.08)	0.0735* (0.064-0.08)	0.072 (0.061-0.081)	0.069 (0.063-0.08)
[89]Y	0.066 (0.059-0.072)	0.07 (0.061-0.079)	0.072 (0.061-0.083)	0.07* (0.063-0.077)	0.066 (0.063-0.069)	0.068 (0.062-0.074)
[66]Zn	147.554 (144.46-157,13)	150.279 (146.88-155.99)	163.5885* (149.05-181,8)	160.9615* (152.24-165.91)	161.033*(156.25-165.52)	160.558*(151.15-170.991)
[90]Zr	0.169 (0.162-0.175)	0.177 (0.177-0.185)	0.1695 (0.155-0.183)	0.1615* (0.151-0.173)	0.155* (0.139-0.167)	0.163 (0.158-0.17)

Data presented as median (25–75); * - Significant difference in comparison to Control group (Kurchum) at p < 0.05; The levels of Be (< 0.081), Bi (< 0.010), Co (< 0.03), Eu (< 0.095), Gd (< 0.060), Hf (< 0.040), In (< 0.008), Nb (< 0.007), Tl (< 0.05), Th (< 0.3), U (< 0.015), and Yb (< 0.07) were lower than the respective limits of detection (LODs).

where the metal level was 9% higher than that in the control group. Hair Zn levels in residents of Akzhar, Borodulikha, and Aksu, were 11, 9, and 9% higher than the respective values in the control site.

The elemental composition of blood was rather different from that observed in the hair samples (Table 3). Be, Bi, Eu, Gd, Hf, La, Nd, Tl, Th, and Yb were detected in very low undetectable concentrations (< LOD). Blood Ba content in residents of Akzhar, Aksu, and Ust-Kamenogorsk was nearly twofold higher than the respective value in residents of control site, Borodulikha, and Karaul, which was statistically significant. A similar situation was observed in the case with lead, where the blood levels in residents of Aksu, Ust-Kamenogorsk and Akzhar significantly exceeded those in residents of control site, Borodulika, and Karaul by 51, 47 and 32%, respectively. However, the blood levels of Sn were significantly 38, 40, and 64% higher in residents of control site, Borodulikha, and Karaul as compared with residents of Akzhar, Ust-Kamenogorsk, and Aksu. As for the blood levels of potentially toxic Ag, these were 39, 36, and 17% higher among residents of the control site as compared with residents of Borodulikha, Akzhar, and Ust-Kamenogorsk, respectively. Notably, no significant difference in blood U levels was detected between the study sites.

Meanwhile, the blood levels of Co were 32 and 29% lower in residents of the control site as compared to Aksu and Ust-Kamenogorsk, respectively. However, the highest levels of blood Cu were detected in residents of control site and Borodulikha, significantly exceeding the respective values in residents of Aksu and Ust-Kamenogorsk by 20 and 17%. Blood Mn levels in the control group were 45, 44, and 38% lower than the respective values in the population of Ust-Kamenogorsk, Akzhar, and Aksu, respectively. At the same time, blood Mo level in residents of Borodulikha was significantly lower than the metal level in the control group by 22%. Blood Cr levels did not differ significantly

Table 3
Blood trace element content (µg/L) in environmentally exposed and non-exposed persons.

Element	Control (Kurchum)	Ust-Kamenogorsk	Akzhar	Aksu	Borodulikha	Karaul
[107]Ag	0.656 (0.607-2.426)	0.562* (0.513-0.606)	0.484* (0.455-0.511)	0.619* (0.521-0.679)	0.473* (0.427-0.519)	0.656 (0.607-3.166)
[135]Ba	4.655 (3.923-6.655)	9.131* (7.604-10.397)	10.0395* (5.936-11.873)	9.168* (8.404-9.596)	4.788 (3.987-5.913)	4.334 (3.651-5.522)
[140]Ce	0.488 (0.37-0.708)	0.608 (0.526-0.72)	0.7275*(0.553-0.915)	0.6245 (0.578-0.678)	0.527 (0.424-0.741)	0.472 (0.37-0.685)
[59]Co	2.628 (2.376-2.984)	3.397*(3.115-3.748)	2.694 (2.304-2.992)	3.468*(3.092-3.996)	2.093 (1.935-2.337)	2.719 (2.496-3.123)
[133]Cs	0.289 (0.229-0.374)	0.333 (0.287-0.418)	0.326 (0.224-0.387)	0.305 (0.277-0.374)	0.309 (0.24-0.41)	0.289 (0.229-0.374)
[53]Cr	24.568 (21.624-27.889)	22.978 (21.079-24.55)	22.349 (19.224-23.938)	22.818 (21.791-24.598)	20.044 (17.855-24.594)	24.568 (21.497-27.889)
[63]Cu	167.841 (117.77-239.75)	142.872*(130.79-150.81)	154.572 (123.72-167.3)	140.421*(136.72-142.96)	144.801(127.85-202.26)	167.841 (117.77-239.75)
[115]In	0.119 (0.107-0.127)	0.117 (0.109-0.147)	0.102*(0.099-0.111)	0.142*(0.128-0.155)	0.114 (0.102-0.124)	0.119 (0.107-0.127)
[7]Li	2.519 (2.427-2.826)	3.356* (3.158-3.544)	3.413* (2.925-3.753)	3.4035* (3.018-3.708)	2.58 (2.375-3.037)	2.472 (2.276-2.796)
[55]Mn	47,452* (35.587-75.385)	69.003* (66.727-71.187)	68.192* (64.936-72.982)	65.549*(63.279-69.898)	52.129 (41.676-62.881)	47.452 (35.587-75.01)
[95]Mo	7.892 (6.811-9.823)	8.176 (7.473-8.774)	6.95 (5.62-8.358)	7.988 (7.383-8.733)	6.455*(5.599-8.456)	7.892 (6.937-9.823)
[93]Nb	0.927 (0.751-1.094)	1.089 (0.986-1.239)	0.919 (0.651-1.086)	1.024 (0.888-1.143)	0.796 (0.529-1.034)	0.925 (0.751-1.094)
[207]Pb	10.371 (7.982-11.916)	15.272*(14.207-16.703)	13.734*(12.32-15.775)	15.621* (14.807-16.442)	10.375 (8.035-12.358)	10.371 (7.982-11.916)
[45]Sc	23.426 (21.186-24.116)	23.544 (22.588-24.213)	24.204 (23.26-24.865)	24.503*(22.106- 26.091)	26.813*(24.761-29.121)	23.458 (21.241-24.272)
[118]Sn	13.208 (9.355-16.01)	9.452*(8.483-10.382)	9.5885*(7.832-12.496)	8.0625*(7.503-8.779)	13.271 (10.332-15.031)	13.208 (9.355-16.01)
[238]U	0.253 (0.168-0.363)	0.297 (0.238-0.367)	0.3215 (0.194-0.392)	0.298 (0.235-0.345)	0.252 (0.132-0.371)	0.251 (0.168-0.36)
[51]V	3.999 (3.332-4.817)	4.61 (4.164-4.86)	4.379 (4.108-5.026)	4.731*(4.203-5.135)	3.291 (2.801-4.337)	4.165 (3.398-4.898)
[184]W	0.124 (0.081-0.486)	0.115* (0.103-0.134)	0.142* (0.103-0.199)	0.1735 (0.132-0.217)	0.098 (0.067-0.251)	0.124 (0.081-0.498)
[89]Y	0.492 (0.431-0.56)	0.598 (0.52-0.674)	0.501 (0.439-0.594)	0.5245 (0.456-0.617)	0.446 (0.362-0.568)	0.497 (0.431-0.582)
[66]Zn	163.171 (132.17-231.84)	186.253 (180.52-197.57)	180.775 (173.97-198.60)	182.088 (177.92-187.45)	157.71 (126.38-204.56)	159.811 (119.95-193.07)
[90]Zr	2.305 (1.798-2.91)	2.711 (2.329-3.089)	2.7765 (2.433-3.139)	2.949*(2.603-3.379)	2.32 (1.51-2.829)	2.305 (1.614-2.91)

Data presented as median (25–75) *Significant difference in comparison to the control group (Kurchum) at P < 0.05; The levels of Be (< 0.030), Bi (< 0.006), Eu (< 0.01), Gd (< 0.01), Hf (< 0.021), La (< 0.014), Nd (< 0.025), Tl (< 0.005), Th (< 0.019), and Yb (< 0.01) were lower than the respective limits of detection (LODs).

between the study sites, except for Borodulikha. As for Zn, blood level in residents of the control site was 14% lower than the respective value in residents of Ust-Kamenogorsk, although this difference was insignificant.

4. Discussion

The obtained data demonstrate that living in a polluted environment results in altered trace element status. However, the elemental composition of hair was found to be more stable as compared to blood. The obtained data contradict the earlier findings indicating that people living in the polluted areas tend to have increased hair levels of toxic trace elements [27,28]. Although hair is unique in terms of its ability to reveal information on past nutritional and environmental exposure [29], hair reflects the content of trace elements in blood at the time of formation [30]. From one hand, hair is stable, easily collectible, and has little requirements on storage and preservation. But on the other hand, hair is subject to exogenous contamination, and there is much natural variation in its composition [31].

Still, the obtained data on the concentration of toxic elements in blood samples are in agreement with earlier international publications. Both Ust-Kamenogorsk and Aksu have smelters within city borders and similar to our findings, earlier studies revealed the elevated blood Pb in the population residing in a vicinity of a copper smelter in Janghang, Korea [32], in San Luis Potosi, Mexico [33] and Karabash, Russia [34]. Available data suggest that smelters play a significant role in anthropogenic contamination of the environment with As, Cu, Cd, Sb, and Zn [35]. Also, they substantially contribute to atmospheric emissions of Cr, Pb, Se, and Ni [36]. Meanwhile, our study failed to confirm the elevated levels of Cr in blood among residents of smelter areas (Ust-Kamenogorsk and Aksu) as residents of the ecologically safe zone had surprisingly higher levels of blood Cr.

Nevertheless, our findings indicate the significantly increased levels of hair Cr in residents of Ust-Kamenogorsk as compared to the control group. However, to interpret the obtained findings accurately, there is a need to acquire the appropriate reference values of hair trace element content since they are inconsistent and subject to regional variation [37]. Despite the absence of systematic data on the reference limits of hair trace element content in Kazakhstani population, we can rely on the reference values obtained for Russian population [38,39] due to the proximity of Pavlodar and East Kazakhstan provinces to Russian Federation. This comparison helps to establish an agreement between the hair levels of trace elements observed in our study and reference values obtained for the Russian Federation. Likewise, an earlier study performed on petrochemical workers from North-Eastern Kazakhstan [40] showed a similar concentration of both essential and toxic trace elements in head hair. Probably, the most accurate conclusion is that there is no chronic overexposure to industry-related pollutants.

Surprisingly, hair V levels in residents of all study sites exceeded the upper reference limit established for the Russian Federation [39]. It may be hypothesized that this disagreement might be due to certain specific features of soil in East Kazakhstan and Pavlodar provinces, which lead to increased accumulation of V in head hair. The earlier study on petrochemical workers originating from North-Eastern Kazakhstan also demonstrated excess hair levels of V, including those in the control group [40]. Since V is released to the environment in large quantities due to the combustion of fossil fuels [41], the increased content of hair V could be partly explained by industrial emissions but also by local geochemical factors. As for the content of other trace elements in head hair, they corresponded to Russian reference values [38,39].

Because trace elements cannot be synthesized in the human body, some of them are vital for human health. There are several routes of how the human body receives metals from the environment and ingestion via "rocks – soils – foods" chain plays a major role. Besides, trace elements may enter the body through inhalation of air,

transcutaneous absorption, and water consumption [42]. For this reason, there is a need to carry out periodic environmental assessments for the contamination with toxic metals. Specifically, a recent study indicates that topsoils in Ust-Kamenogorsk display strong polymetallic pollution and have extremely high contamination with cadmium (Cd), strong contamination with lead, moderate contamination with Zn, and moderate to low contamination with Cu. It was found that lead and Cd were bound to acid-soluble fractions and were the most bioavailable of all studied elements [6]. An earlier study confirmed increased contamination of soils in Ust-Kamenogorsk with Zn and established that it was distance-dependent [43].

Our study identified a significant decrease in blood Cu with a simultaneous increase in hair Cu among the population of Ust-Kamenogorsk and Aksu. This phenomenon might be attributed to direct accumulation of Cu from an atmospheric air, which contains it in excessive amounts due to the proximity of copper smelter [35]. Meanwhile, decreased blood Cu levels may originate from Cu deficiency due to increased environmental load with toxic metals that act as Cu antagonists [44]. The sample of such metals could be made of lead, which is presented in the soil of Ust-Kamenogorsk in biologically-active form. Besides, according to our findings, people residing in Ust-Kamenogorsk and Aksu have significantly elevated blood lead levels. However, more research is needed on other parameters of Cu status before any definite conclusions could be drawn.

Also, reduced Cu levels in the blood cause other consideration since Cu is mainly a key-element of ceruloplasmin, which carries more than 95% of Cu in human plasma [45]. One of the functions of ceruloplasmin is to oxidize Fe^{2+} (ferrous iron) to Fe^{3+} (ferric iron). Along with transferrin, ceruloplasmin takes part in Fe transport and thus, decreased blood Cu levels may lead to disturbed Fe metabolism [46]. Although Fe was not among the elements investigated in this study, Fe-deficient anemia is a major public health problem in Kazakhstan [47] and reduced Cu levels in the blood might contribute to this.

In the present study, the population of Ust-Kamenogorsk, Akzhar, and Aksu was characterized by a twofold increase in blood Ba content as compared with the population of other study sites. Ba is extensively used in various industrial purposes but also is known to be a companion of Cu and Au ores [48]. At present, Kazakhstan possesses one of the largest explored Ba deposits in the world and enters the top 10 of Ba producers [49]. Since Ba is not processed in any of the studied settings, excessive blood levels in local residents are probably best explained by natural geochemical conditions (Akzhar) and by the processing of other ores (Ust-Kamenogorsk and Aksu).

Elevated Ce blood levels significantly exceeding those of control site by 49% was identified in residents of Akzhar, which locates just at the border with the Semipalatinsk Nuclear Test Site. Although Ce is mined in East Kazakhstan, Pavlodar region – to which belongs Akzhar – does not produce it. Ce is a known polishing compound and is used in the production of high-quality optical surfaces, which does not happen in the Pavlodar region. Besides, Ce has automotive application as an additive to Diesel fuel [50]. As soon as there is no association between heavy traffic or use of Diesel and related exhaustive in Akzhar village, the actual cause of elevated Ce blood levels could not be established. However, residents of other study sites demonstrated Ce blood content very similar to that in the control site.

As for radioactive trace elements, no significant difference in blood U levels was detected between the study sites, and Th was identified in undetectable concentrations. Unfortunately, no comprehensive assessment on radio-contamination of areas around the former SNTS was found in available literature databases. Still, Yalaltdinova and co-authors evaluated concentrations of U and Th in natural environments of Ust-Kamenogorsk [51]. The highest U content was observed in snow cover, while the highest Th content was noted in top soils and distance-dependence in relation to the location of the thermal power station and the polymetallurgical plant was established. The authors conclude that atmospheric air is the most likely route of entry for Th and U, but in the

present study, the head hair levels of both elements were in un-detectable amounts.

5. Conclusions

The conducted biomonitoring indicates that residency in two industrial settlements of Kazakhstan – Ust-Kamenogorsk, and Aksu – has a significant impact on the contents of trace elements in the human blood. In particular, the blood Ba content was nearly twofold higher than that in the control site, while the blood levels of lead exceeded those in control site by 51% for Aksu and by 47% for Ust-Kamenogorsk. Besides, an alteration of Cu status in people living near the copper smelter was identified, which manifested as a significant decrease in blood Cu with a simultaneous increase in hair Cu. This might be attributed to Cu deficiency originating from an increased environmental load with Pb, which acts as Cu antagonists, although more studies are needed to check this hypothesis.

Meanwhile, the elemental composition of head hair was characterized by greater stability between the study sites as compared with the composition of blood. Still, residency near the former Semipalatinsk Test Site could be considered as safe in terms of toxic metal exposure since hair and blood concentrations of most toxic, and potentially toxic trace elements were similar to those observed in the control site, except for Akzhar that demonstrated elevated Ce blood levels. To conclude, the environmental status of studied industrial settlements appears to be rather adverse and requires further investigation along with the application of pollution shortening measures.

Author contributions

Yu. Semenova, L. Pivina, and G. Bjørklund conceived and designed the present study. T. Belikhina, A., Lipikhina., A. Tinkov, Y. Zhunussov, T. Bulegenov, A. Abisheva, M. Zhanaspayev, A. Skalny, M. Dauletyarova, and N. Glushkova contributed to discussing the statistical method and the interpretation of our findings as epidemiological, chemical, and public health specialists. Yu. Semenova and L. Pivina analyzed the data and wrote the paper. All authors contributed to revisions of the manuscript and critical discussion.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgments

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