THE ESSENTIAL AND TOXIC EFFECTS OF TRACE ELEMENTS IN THE BIOLOGICAL TISSUES OF PREGNANT WOMEN AND NEWBORN BABIES (AN ECOLOGICALLY UNFAVOURABLE REGION)

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ABSTRACT

Ecological conditions in the Urals are unfavorable. In the Sverdlovsk region, every second pregnancy and in Yekaterinburg every third pregnancy burdened of obstetric and gynecologic pathology. It makes us pay a special attention to the reasons of the increased perinatal morbidity and mortality. The aim of the research was to estimate the levels of macro and trace elements: Fe, Ca, Mn, Cu, Zn, Cd, Pb, Cr, Ni of 156 pregnant women and their newborn babies inhabiting an industrial city, where the environment is polluted with heavy metal compounds. It was found that the women had low indices of ecological valency, pregnancy complication and break of reproductive functions (hestoses, anemia, threat pregnancy interruption). Inspection of cases revealed chronic hypoxia (81.2%), Fe-deficiency anemia (50.4%), gestosis (29.9%), extragenital diseases of infectious inflammatory character (65%), chronic pyelonephritis (18.8%), hypertension (13.7%).

All inspected women (megacity) had higher levels of trace elements: Cu, Zn, Cd, Pb, Cr, Ni in the placenta tissue ($p < 0.05$) and the deficiency of the essential elements Mn, Mg and Fe ($p < 0.01$). Higher levels of Cu, Cd, Pb were observed in the blood serum. The newborn babies had higher levels of Cu and Pb in the blood serum. Direct correlations were marked between Cd in the megacity environment and in placenta of pregnant women ($R = 0.86$, $p = 0.041$). Average correlation was marked between Pb in the megacity environment and placenta of pregnant women ($R = 0.34$; $p = 0.038$). A strong reverse correlation was observed between heavy metals in the city environment (Cu, Zn, Pb) and body mass of newborn ($R = -0.98$; $R = -0.98$; $R = -0.80$ respectively, $p = 0.034$). Reverse correlation was marked between Cd and the fetal growth ($R = -0.79$; $p = 0.037$). We marked absence of significant distinctions between the basic and the control group in Cd levels in the blood of healthy newborn babies (0.003 ± 0.001 and 0.002 ± 0.001 mkg/mL, respectively). This evidenced about active barrier function of placenta of healthy women. Significant quantities of Pb were marked in the blood serum of newborn. Barrier function of placenta for Pb was not noted. The placenta passes Cu and Zn to the blood of newborn. The combined effect of macro- and microelements through the system mother–placenta–newborn is unfavorable for the fetus.

Pregnant women (megacity) – a group of high risk by the prenatal development (intra-uterine hypoxia and the fetal growth restriction) – and their newborn babies were at risk of developing pathologies provoked by the transplacental ability of toxic elements.

Keywords: Blood serum, macro- and microelements replaceable, newborn, placenta, pregnant women, trace elements.

1 INTRODUCTION

An attempt to estimate ecological risks for the population health (combined effects of pathogenic environmental factors which cause injuries and illnesses) has been seen in solutions of various international organizations [World Health Organization (WHO),

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United Nations Environment Programme] and governments. WHO marks the growing injurious effect of the environmental pollution on the health of the population. Developed countries exist in ecologically adverse conditions of industrially large areas. An actual problem is the development of the safety conception aimed at the elimination of the environmental danger [1–5].

According to official statistics, population health in Russian regions is aggravated [6–8]. There is an increasing trend of depopulation. The contemporary extremely negative demographic situation in the Russian Federation is characterized by a decreased population number due to the low birth rate and increase of perinatal morbidity and mortality [9–13]. The mortality rate of babies in Russia exceeds three to four times that of other European countries [14].

The Ural region has long ago become a zone of ecological risk due to a strong pollution with heavy metals and radionuclides [15, 16]. The degradation of natural and anthropogenic modified ecosystems is reflected in qualitative changes of the population gene pool. The medical situation is unfavorable: every second pregnancy in Sverdlovsk region in the Urals and every third pregnancy in Yekaterinburg has an obstetrical or gynecological pathology [17]. It is known that a state of the fetoplacental complex is responsible for the bearing and birth of a healthy child [18–20]. Estimation of the anthropogenic pollution on reproductive system of women and of system–mother–placenta newborn is very important for the health of future generations.

We observe the growth of ecologically dependent pathology in women and children and a high-fetal risk at various pregnancy terms. Health protection of women and their newborn especially, in ecologically unfavorable regions, including the Urals, is a very important clause for the national safety.

Aim: (i) To study the levels of macro- and trace elements in the biological substrata of the 'mother–placenta–newborn' system of women inhabiting a megacity. (ii) To estimate the effect of environmental pollution on women during their gestation period. (iii) To show the presence or absence of the barrier function of the placenta against heavy metals.

2 HYGIENIC EVALUATION OF THE ENVIRONMENT IN SVERDLOVSK REGION

The hygienic situation of the environment in the Urals is unfavorable. The Ural region is in first place among economic regions based on the quantity of total emissions of harmful chemical substances in atmosphere [17, 21]. Sverdlovsk region is situated in the Eurasian continent at the boundary of Europe and Asia, in the northern and middle parts of the East European and West Siberian plains. It is one of the oldest mining regions in Russia with intensively developed ferrous non-ferrous metallurgy and chemical industry. The population (approximately 4 million) is affected by hazardous environmental factors. The data of 'Sverdlovsk Center of Hydrometeorology and Environment pollution Monitoring' indicate that the unfavorable ecological situation in Yekaterinburg may have an effect on the population health and the demography [21].

2.1 Regional technogenic risk factors

Over 2.7 million people are affected by toxicants of the first class (Cd, As, Hg, Pb, Cr); over 2.3 million people are affected by toxicants of the second and third classes (Co, Ni, Cu, Zn, Mg, Fe, Mn). Risks: premature deaths of adults due to multimedia pollution with Pb, nephropathy and oncology diseases cased by Cd. Oncology risks due to multimedia pollution with As, Cd, Pb result in a lower birth rate and demography in the region.

Table 1: Average annual concentrations of heavy metals (air pollution) (data from the State Report on the Environment State and the Effect of Environmental Factors on the Population Health in Sverdlovsk Region in 2009–2010) [21].

Trace elements	Yekaterinburg, industrial city, (background average annual, mg/m^3)	Sverdlovsk region, non-industrial areas (background average annual, mg/m^3)	Maximum allowable concentration, mg/m^3 [a]
Cu	0.08	0.04	0.0003
Zn	0.27	0.023	0.0002
Mn	0.07	0.014	0.001
Ni	0.04	0.005	0.0001
Cr	0.08	0.006	0.0015
Cd	0.01	0.0002	0.0000
Pb	0.16	0.006	0.0005
Fe	2.12	0.10	0.0004
Mg	0.27	0.03	0.0008

[a] Government standard Russia Federation: GOST17.2.1.03-84.Nature protection. Atmosphere. Terms and definition for air pollution control; GOST 22.1.02-97. Safety in emergencies. Monitoring and forecasting. Terms and definition.

The medical and demographic situation is affected by the following factors: chemical and radiation loads, social welfare level, social tension, industrial development of the area. During the past few years, the leading factor is the complex chemical load (75.2% of the population is affected) caused by the polluted air, soil, drinking water and food. During the last 10 years Yekaterinburg with its industrial enterprises and intensive traffic is in the list of the most air polluted cities dangerous for the health of its residents [21]. In 2006–2010 high levels of air pollution with heavy metals (Pb, Co, Cd, Cu, Mn, Fe, Ni, Cr, Zn) were registered in all districts of the city.

Table 1 gives the data of 'Sverdlovsk Center of Hydrometeorology and Environment Pollution Monitoring', which is an evidence of the unfavorable ecological situation in Yekaterinburg [21]. In 2010, the quality of the drinking water in the centralized water-supply system decreased, which is primarily due to higher concentrations of Cl-organic compounds, Fe, Mn, Al, Cd, Pb, etc. The city soil was polluted with heavy metals of the 1 and 2 class of danger: Cu – 58 times exceeded the background level, Ni – 20 times, Pb – 18, Zn – 6.4, Cr – 8.5, Co – 2.4, Cd and Mn – 3.1, Fe – 1.2 times. The contribution of heavy metals to the soil pollution in Yekaterinburg in 2010 was the following: Cu – 15%, Ni – 34%, Zn – 14%, Cr – 19%, Pb – 18%. The main sources for the heavy metals were the traffic, industrial enterprises, industrial and waste products.

2.2 Medical and demographic situation

Unfavourable hygienic factors and economic indices cause stable negative trends in the population health in Sverdlovsk region [17]. The total morbidity has grown 11.5% compared with the many-year average level and 4.8% compared with 2009. In the morbidity structure, the first place is occupied by respiratory system diseases (26.1%), the second by blood circulation system diseases, the third by traumas and poisoning (7.4%). Among the morbidity causes the first place is occupied by blood circulation system diseases (54.1%), the second by tumors (15.7%) and the third by traumas and poisoning (12.9%).

The reproductive health of women is one of the primary problems in Sverdlovsk region. In 2010, the risk group for ecologically determined health disturbances included pregnant women dwelling in heavily polluted cities. Every third pregnancy was complicated with anemia, diabetes mellitus increased by 5.3% compared with the many-year average, the number of human immunodeficiency virus–infected people increased 12.2 times during the last 5 years. In 2010, blood circulation diseases increased by 1.5% compared with the many-year average. Premature deliveries decreased by 3.8% (against 5.8% in 2009), emergency deliveries was reported in 90.2% of the cases (89.5% in 2009).

In 2010, the indices for the prematurely born (6.9%) and newborn weighting over 2.5 kg (93.01%) were stable. The structure of the newborn morbidity was the following: certain states in the perinatal period – 95.4%, congenital anomalies – 2.8%, infection diseases specific for the perinatal period – 1.8%. Morbidity during the first year of life increased 5.9% compared with the many-year average or 12% compared with 2009. As usual, there were about three diseases per year for one child during the first year. These were respiratory system diseases (39.4%), individual states of the perinatal period (21.9%), diseases of the neural system (6.7%). The leading causes for the infant mortality during the first year were individual states of the perinatal period (40.9%), congenital anomalies (20.3%), respiratory system diseases (6.9%), infection and parasitic diseases (4.2%), traumas and poisoning (10%) [17]. Among the children dead before 14 years of age, 60.1% were those on the first year of life. Mortality between 0 and 14 years grew by 5.7% in 2010 compared with 2009 [17].

As participation of the essential (Fe, Mg, Ca, Mn, Cu, Zn, Ni) and toxic (Cd, Pb, Cr) microelements in the course of pregnancy is doubtless, the problem of their toxicity for an embryo and fetus is very important [22, 23]. A growing number of women inhabiting megacities are affected by various combinations of these elements. A good state of the fetoplacental complex is responsible for the bearing and birth of a healthy child [18–20]. At present, there are no exact data on adaptation to trace elements [12, 15]. Shortage of facts does not allow to uniformly explain the mechanisms underlying participation of trace elements in homeostasis. In conditions of the environmental pollution with hazardous compounds responsible for the toxic effects on the embryo – and gonads – the prevention of fetoplacental insufficiency requires early diagnostics and preventive measure [11, 12, 16, 20, 24]. Publications on the effect of trace elements in the mother–placenta–newborn system on the homeostasis processes are also absent. Knowledge of the correlation between fetal pathology and the factors responsible for it can help to effectively treat and prevent pathologies.

3 CASES AND METHODS

The research was done in the obstetric clinic of the Maternity Hospital No. 1 in Yekaterinburg. We made a complex standard-laboratory inspection of 156 pregnant women at the age of 17–42 and of their newborn (blood indices) and a retrospective analysis of ambulatory cards of pregnant women, birth histories, and newborn development histories (anamnesis) were carried out. The choice for the inspection included the following: no women with heavy extragenital pathology, obstetric traumas, abnormal parturition. The group included non-smokers, non-consumers alcohol and narcotic. There were no professions with harmful working conditions.

The state of the newborn was evaluated on the Apgar score (WHO recommendation) 1 and 5 minutes after birth: 8–10 – good state; 7 – between normal and pathology; 6 – light asphyxia; 5–4 – heavy asphyxia neonatorum or absence of positive dynamics.

The object of research was the biological system – mother–placenta–newborn. For the analysis, blood was taken from the cubital vein before the parturition, while blood from the placenta and the umbilical cord was taken during the parturition. Blood indices were investigated in all women in the third trimester on the automatic Bio-Medical Analyzer BC-5800c Shenzhen Mindray (China).

A complex prenatal ultrasonic inspection of pregnant women included fetometry, evaluation of the fetal biophysical profile, dopplerometry of the blood stream in the umbilical cord arteries. For the echographic and dopplerometry measurements, we used the ultrasonic scanner Aloka-SSD-1400 (Japan) and Sonoline G40 Siemens-Acuson scanner (three sensors, cardiac activity sensor) (Germany). Dopplerometric inspection of the blood stream during the second and the third trimester allowed to predict intrauterine hypoxia of middle and heavy degree and intra-uterine growth restriction [25, 26].

The levels of microelements Fe, Ca, Mg, Mn, Ni, Cr, Zn, Cu, Cd, Pb in placenta tissues, blood serum of women, in the umbilical blood of the newborn were analyzed in triplicate by atomic absorption spectrophotometry Perkin Elmer Analyst 1000. Separate and disposable sterilized plastic syringes were used for blood collection. A blood sample was left standing for 1 hour to coagulate; serum was separated by centrifugation for 10 minutes at 2000 rpm, transferred to a 5 mL polystyrene tube and stored at –18–20°C until the analysis was over.

The protocol was approved by the Medical Ethics Committee of the Ural State Medical Academy in Yekaterinburg, and discussed in detail with each volunteer before she gave her written informed consent to participate in the research, according to the tenets of the Declaration of Helsinki. The confidentiality of the collected data is guaranteed in the protocol.

A statistical analysis was carried out using STATISTICA. The results were shown as a mean ± standard errors of mean. Parameters showing Gaussian distribution were analyzed by Student's t test. Mann–Whitney U test was used for parameters showing non-Gaussian distribution. The correlation between variables was evaluated by Pearson's correlation coefficients or Spearman's rank correlation coefficients were used to relate trace elements concentration, body mass, fetal growth and medical data. The distinctions between the samples were considered to be statistically significant at $p < 0.05$.

4 RESULTS AND DISCUSSION

The basic and the control groups were formed by random sampling, taking into account the of ecological conditions of their residence. The basic group was 127 pregnant women and their 127 newborn, constantly living in Yekaterinburg – a large industrial center in Russia. The control group was 29 women constant residents of non-industrial areas in Sverdlovsk region and their 29 newborn.

In the basic group (Yekaterinburg residents), 81.25% had complicated obstetric and gynecologic anamnesis, somatic pathology and pregnancy complications. Approximately 65% had various extragenital diseases of infectious inflammatory character (Table 2).

For the anemic women (megacity) (50.4%), threats of pregnancy interruption (13.7%) and hypertension unconnected with pregnancy were noted in 16%. Approximately 18.8% of women had chronic pyelonephritis and 29.9% had gestosis.

Table 2: Inspected pregnant women and their newborn babies.

Totally inspected	Control group, n = 29. Sverdlovsk region (non-industrial areas)	Basic group, n = 127. Yekaterinburg (industrial city)
Pregnant women n = 156 (17–42 years old)	20 (69%) – physiological pregnancy and delivery	24 (18.75%) – physiological pregnancy and delivery
	Pregnancy complications: 31% – complicated obstetric and gynecologic anamnesis 50% – Fe-deficiency anemia 25% – chronic pyelonephritis 25% – gestosis 12.5% – hypertension 100% – extragenital infections	**Pregnancy complications**: 103 (81.25%) – complicated obstetric and gynecologic anamnesis 65% – extragenital diseases of infectious-inflammatory character 13.7% – menace of pregnancy interruption 16% – hypertension 64(50.4%) – Fe-deficiency anemia 38(60%) – slight anemia 18(28%) – average anemia 8(12%) – heavy anemia1 18.8% – chronic pyelonephritis 29.9% – gestosis
Newborn n = 156	Control group, n = 29 92.3% – proportional physical development 7.7% – intra-uterine growth restriction 30.8% – chronic hypoxia Average mark on the Apgar score (newborn, 1 minute) – 8.7 ± 0.5	Basic group, n = 127 24(18.7%) – healthy children 75% – proportional physical development 25% – intra-uterine growth restriction 36.1% – born premature 104 (81.2%) – chronic hypoxia 73 (24%) – slight anemia 30 (10%) – average anemia 5 (4%) – heavy anemia 10 (10%) – purulent-septic diseases Average mark on the Apgar score (newborn, 1 minute) – 6.8 ± 0.34

In the control group (non-industrial areas), physiological pregnancy and delivery were observed in 69% of women.

Complicated obstetric anamnesis and various complications of pregnancy were marked in 31%. Approximately 100% from the control group had extragenital infections. Complications of pregnancy were the following: Fe-deficiency anemia – 50%; chronic pyelonephritis – 25%; gestosis – 25%; hypertension unconnected with pregnancy – 12.5%.

In the basic group (industrial city), the number of complicated pregnancies and deliveries exceeded the frequency of complications among the newborn: immaturity syndrome of respiratory disturbance predominated among the newborn. In the basic group, 18.7% was born healthy, chronic hypoxia of various degrees was observed in 81.2%.

For the newborn babies, light hypoxia cases exceeded those in the control group by 4.1 times; average degree cases – 2.0 times; every fifth child had heavy hypoxia. In the basic group, 75.0% of children had proportional physical development, 25.0% of children had intra-uterine growth restriction and 36.1% of these newborn babies were born premature (Table 2).

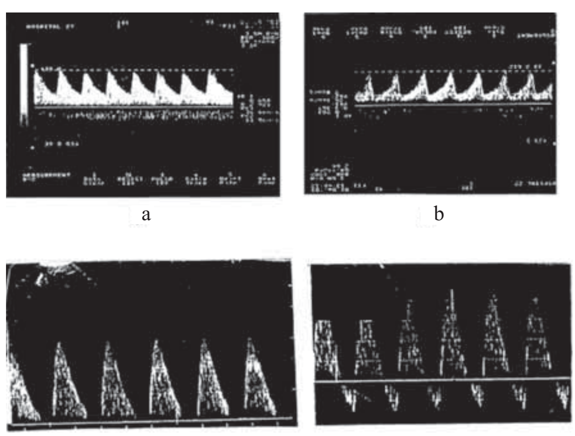
In the control group, 92.3% of children had proportional physical development and 7.7% had intra-uterine growth restriction. Chronic hypoxia was observed in 30.8% of the newborn from the control group. In the control group there were no premature births [25, 26]. We see from the table that considerably worse obstetric indices were observed in women living in ecologically unfavorable conditions in comparison with the women whose organisms were not affected by hazardous anthropogenic factors. Especially worse was the state of fetus and newborn – they exhibited the highest degree of hypoxia and intra-uterine growth restriction.

In somatically healthy women without complicated pregnancy no pathological curves of the blood-current in the umbilical cord artery were registered (Fig. 1a).

Pregnant women with prenatal fetal pathology exhibited a lower diastolic component of the blood flow in the umbilical cord artery, and apparition diacritics dimple in the phase of early diastole (Fig. 1b). In cases of heavy prenatal fetal pathology – zero and reverse diastolic component of the blood flow in the umbilical cord artery were registered – a characteristic sign of a heavy disturbance of fetoplacental blood circulation (Fig. 1c and Fig. 1d).

Thus, compared with other regions, all pregnant (megacity) women have higher levels of trace elements: Cu, Zn, Cd, Pb, Ca, Cr, Ni in the blood serum and in placenta tissue ($p < 0.05$). This fits results of other authors [5, 10, 19, 27–32]. The levels of the essential macroelements – Mn, Mg and Fe were significantly lower ($p < 0.01$).

Concentrations of cadmium and lead in the blood (Cd = 0.03 ± 0.006; Pb = 0.31 ± 0.07) and in placenta (Cd = 0.084 ± 0.014; Pb = 0.62 ± 0.8) of pregnant (megacity) women significantly exceeded maximum possible concentration of other technogenic territories



a b

c d

Figure 1: Dopplerometric indices of pregnant residents (III trimester): (a) healthy fetus; (b) initial stage of placenta insufficiency; (c) absence of diastolic component in all heart cycles; (d) reverse diastolic component of the blood flow in all heart cycles.

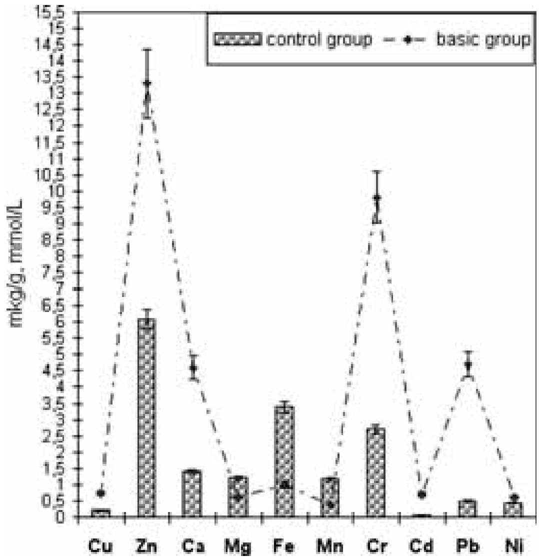


Figure 2: Trace elements in placentary tissues of megacity (basic group) and non-industrial area (control group) residents (Cd, Pb – mkg/g × 10).

(by the European standard) [4, 8]. Somatically healthy women of Yekaterinburg (basic group) had significantly higher concentrations of heavy metals in placental tissues than somatically healthy women out of the control group (Cu – 1.8 times, Zn – 2.4 times, Cd – 14.0 times, Pb – 12.4 times) (Fig. 2).

A direct correlation was revealed between the levels of Cd in the megacity environment and in the placenta of pregnant women ($R = 0.86$, $p = 0.041$). At the same time placenta was a barrier for the penetration of high concentrations of cadmium into the fetal organism. In the umbilical blood of the newborn babies there was less Cd than in the mother's blood (women from megacity and from non-industrial areas) (Table 3).

We marked absence of significant distinctions between the basic and the control group in Cd levels in the blood of healthy newborn babies (0.003 ± 0.001 and 0.002 ± 0.001 mkg/mL – accordingly, $p = 0.01$). This evidenced about active barrier function of placenta of healthy women. Placenta reduces Cd levels in blood of newborn babies in – 10 times in megacity conditions and in – 2.5 times in non-industrial areas.

Correlation had average values between the levels of Pb in the megacity environment and in placenta of pregnant women ($R = 0.34$; $p = 0.038$). Barrier function of placenta for Pb was not noted. Permeability of placental barrier to toxic Pb was high activity. Significant quantities of Pb were marked in the blood serum of newborn. Placenta pass along Cu and Zn to the blood of newborn (Table 3).

Correlation analysis showed that the distribution and accumulation of heavy metals in the fetal and newborn organism were significantly dependent on the concentration of metals in the mother's blood. For Cd levels, there was a significant relationship between the blood serum and placenta tissue of pregnant women ($R = 0.567$, $p = 0.032$) but there was no correlation in the mothers–placenta–newborn blood ($R = 0.098$, $p = 0.048$) and mother's blood–newborn's blood systems ($R = 0.140$, $p = 0.041$).

Table 3: Heavy metals in the biological substrata of somatically healthy women from Yekaterinburg (1) and non-industrial areas of Sverdlovsk region (2).

Heavy Metals (mkg/ mL)	No	*N*	a) Mothers blood serum	b) Placenta	c) Newborns blood serum	Student's *t*-test	p-value
Cu	1	27	1.4 ± 0.16	0.72 ± 0.067	0.72 ± 0.14	a) T1-2 = 7.03 > Tst = 2.7	0.01
	2	16	0.26 ± 0.025	0.22 ± 0.022	0.2 ± 0.02	b) T1-2 = 6.7 > Tst = 2.7	0.01
						c) T1-2 = 4.43 > Tst = 2.02	0.05
Cd	1	27	0.03 ± 0.006	0.07 ± 0.007	0.003 ± 0.001	a) T1-2 = 4.17 > Tst = 2.7	0.01
	2	16	0.005 ± 0.001	0.006 ± 0.001	0.002 ± 0.001	b) T1-2 = 9.14 > Tst = 2.7	0.01
						c) T1-2 = 2.0 < Tst = 2.02	0.01
Zn	1	27	4.73 ± 0.88	13.34 ± 1.45	3.18 ± 0.42	a) T1-2 = 0.7 < Tst = 2.03	0.05
	2	16	5.44 ± 0.44	6.1 ± 0.49	5.79 ± 0.55	b) T1-2 = 4.8 > Tst = 2.7	0.01
						c) T1-2 = 6.2 > Tst = 2.7	0.01
Pb	1	27	0.31 ± 0.07	0.47 ± 0.139	0.15 ± 0.04	a) T1-2 = 3.4 > Tst = 2.7	0.01
	2	16	0.063 ± 0.021	0.05 ± 0.014	0.04 ± 0.002	b) T1-2 = 3.02 > Tst = 2.7	0.01
						c) T1-2 = 2.8 > Tst = 2.0	0.02

Disbalance of trace elements in homeostasis of pregnant women showed that the system mother–placenta–newborn was a single functional structure that is responsible for the health of progeny.

We marked a spatial correlation between newborn pathology and the environment pollution with heavy metals (R = 0.63, p = 0.041). In the basic group (Fe-deficient anemic mothers) placenta insufficiency was accompanied with the deficiency of essential elements: Fe, Cu, Ca, Zn, Mg in the blood of the newborn during the first hours after birth. In the blood of those children Cd levels increased five times (0.02 ± 0.001 mkg/mL), concentrations of lead –1.9 times (0.29 ± 0.07 mkg/mL) against the background of lower levels of the essential microelements: Cu (0.68 ± 0.085 mkg/mL), Zn (1.4 ± 0.95 mkg/mL), Fe (0.81 ± 0.05 mkg/mL) and Mg (14.5 ± 0.06 mkg/mL) compared with the children born by somatically healthy mothers (Fig. 3).

The development of pathological processes that caused embryo and fetus suffering significantly depended on the state of microelement metabolism, which frequently affected other metabolic processes in an organism. Thus, in the umbilical-cord blood of children with prenatal hypoxia (81.2%), we observed increased levels of copper against the background of lower levels of the essential zinc, iron, calcium, magnesium ($p < 0.05$) (Fig. 3). Fe levels were up to 0.65 mkg/mL in cases of heavy chronic hypoxia ($p < 0.05$).

The disbalance of trace elements in a newborn's blood also resulted from the entry of toxic heavy metals (cadmium and lead), concentrations of which correlated with the degree of hypoxia ($p < 0.05$). Zn, Fe and Mg are known to induce the synthesis of metallothionein, which bonds with the excessive Pb, Cd [33, 34]. As the levels of these metals were low in the blood of the newborn, this effect was absent (Fig. 3). The deficiency of the essential elements (Cu, Fe, Zn, Mg, Ca) and the selective accumulation of toxic microelements (Cd, Pb) in the umbilical cord blood were the reason for the prenatal fetus suffering, low body mass at birth,

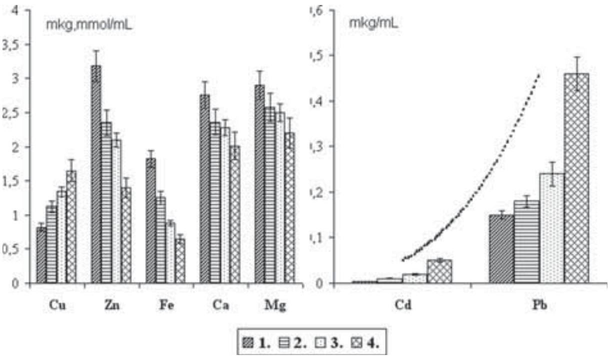


Figure 3: Trace elements in the newborn babies the umbilical cord blood. (1) – healthy, (2) – intrauterine light hypoxia, (3) – hypoxia average degree, (4) – heavy hypoxia.

growth retardation [23, 27]. This conclusion was supported by our research on the physical development and health of the megacity newborn. The established correlations between the levels of heavy metals and indices of physical development provide an evidence of an injurious complex effect of high concentration of Cu, Zn, Pb on the body mass ($R = -0.98$; $R = -0.98$; $R = -0.80$ respectively, $p = 0.034$) and of Cd on the fetal growth ($R = -0.79$; $p = 0.037$). This effect caused the failure of early adaptation of the newborn and subsequent health deviations. The disturbance of growth and development of the fetus and the newborn was often the reason for the prenatal death, difficult early neonatal adaptation and many diseases in future [14, 22, 30, 32, 35].

5 CONCLUSION

The reproductive health of women and health of their newborn babies (in ecologically unfavorable regions) is one of the primary problems in the Urals. The most important factors responsible for the high obstetric risk during pregnancy and their influence on the demography were the ecological situation and population health in the industrial Urals. A direct correlation was revealed between Cd levels in the city environment and in placentas of its pregnant residents ($R = 0.86$, $p = 0.041$). For Pb, the relationship had average values ($R = 0.34$; $p = 0.038$). The ecologically unfavorable urban environment promoted changes in physiological and biochemical processes underlying prepathology and pathology.

Over 81% of inspected megacity females had somatic pathology. They had low indices of ecological valency, disturbance of reproductive functions and pregnancy complication (gestoses, anemia, menace of pregnancy interruption). They had high levels of fetal hypoxia (81.2%). We discovered the following disturbances: Fe-deficiency anemia (50.4%), gestosis (29.9%), extragenital diseases of infectious inflammatory character (65%), chronic pyelonephritis (18.8%), hypertension (13.7%).

It is known that in the embryonic and fetal pathological development the trace elements metabolism plays a great role, often influencing the whole metabolic processes. All pregnant Yekaterinburg women had higher levels of trace elements: Cu, Zn, Cd, Pb, Cr, Ni in placenta tissue ($p < 0.05$) and low levels of the essential elements Mn, Mg and Fe ($p < 0.01$), higher levels of Cu, Cd, Pb in the blood serum. Their newborn had 3.8 times higher levels of Pb in the blood serum than in the control (non-industrial areas). This provided the evidence of increased permeability of the placenta barrier for Pb. Observed Cd concentrations in the blood serum of the megacity newborn and the newborns from non-industrial city did not significant differences. It is necessary to note the expressed barrier function of a placenta to cadmium.

The high extragenital morbidity among megacity residents, frequent complications during pregnancy and parturition, the observed disbalance of trace elements in homeostasis showed that the system 'mother–placenta–newborn' is a functional structure dependent on ecological environmental conditions and is responsible for the health of the progeny. Fetoplacental insufficiency, complicated pregnancy and parturition, unfavorable postnatal complications affected newborn babies.

We marked an increasing trend of newborn with small body mass (intrauterine hypoxia), congenital development defects and neural system diseases. Increased newborn morbidity rates showed that the new generation of babies is physiologically and psychologically weak and there is a threat of increasing depopulation processes in the native population. In conditions of the environment pollution with hazardous compounds responsible for the embryo – and gonad – toxic effects, a prevention of fetoplacental insufficiency is impossible without early diagnostics and preventive measures.

We propose that pregnant women (megacity) – a group of high risk by the prenatal development (intra-uterine hypoxia and the fetal growth restriction) – and their newborn babies were at risk of developing pathologies provoked by the transplacental ability of toxic elements. Besides medical and biological programs, complex ecological and social programs should be put into practice.

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