










## Influence of the Environment on the Chemical Element Content in Women's Blood

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### ABSTRACT

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#### Keywords:

*toxic elements, industrial emissions, environmental contamination, public health, environmental health risk*

This study investigates the impact of industrial emissions on the concentration of toxic elements, such as barium, strontium, arsenic, thorium, and uranium, in the biological tissues of pregnant women residing in Kazakhstan's industrial regions. The study focuses on the potential health risks to both the mothers and their developing fetuses, given the ongoing environmental contamination due to rapid industrialization. 67 pregnant women from various districts in the Akmola region were selected for this cross-sectional study. Biological samples, including placenta and umbilical cord blood, were collected and analyzed using instrumental neutron activation analysis and scanning electron microscopy techniques. Data on environmental and occupational exposure were gathered through questionnaires. The barium, strontium, arsenic, thorium, and uranium concentrations were statistically analyzed using Microsoft Excel and STATISTICA to assess correlations with health outcomes. The findings showed elevated concentrations of barium and strontium in both the placenta and umbilical cord blood, indicating significant exposure through environmental contamination. Arsenic and uranium were also detected in smaller amounts, with localized variations across different regions. The study found a strong association between higher concentrations of these elements and adverse pregnancy outcomes, such as anemia, preeclampsia, and developmental anomalies in the fetus. This study highlights the critical environmental health risks of industrial emissions in Kazakhstan's rapidly developing regions. The transplacental transfer of toxic elements poses serious risks to maternal and fetal health, increasing the incidence of pregnancy-related complications. These findings emphasize the need for stricter environmental regulations and public health interventions to mitigate industrial pollution and safeguard vulnerable populations.

## 1. INTRODUCTION

A key reason for the increase in the morbidity of pregnant women and their children is the significant exposure to pollutants from the environment. These substances are widespread and can be transmitted through the air or water, soil, and food, posing serious health threats. Over the past century, rapid industrialization has led to the careless exploitation of the Earth's natural resources, exacerbating the global pollution problem [1].

In some countries, economic growth has occurred over the past two decades, contributing to an increase in the pace of industrialization. Such countries include Kazakhstan. The energy sector and metallurgy make up the largest share of Kazakhstan's industrial sector and are sources of pollution. According to researchers, in 2019, 10 of the 14 major cities in Kazakhstan had a high level of air pollution, associated with increased emissions of pollutants from enterprises [2]. Earlier,

researchers [3] found an increase in the levels of barium (Ba), manganese (Mn), lead (Pb), vanadium (V), and zinc (Zn) in the blood of residents of Aksu and Ust-Kamenogorsk (Eastern Kazakhstan). An increased content of heavy metals was found in the hair of people living in the Caspian region of West Kazakhstan, where oil and gas fields are located [4]. These few studies show the tense environmental situation in most regions of Kazakhstan. Thus, it is necessary to study the effects of toxic substances on the health of local people more carefully.

Metals are the most common toxic industrial waste among all layers of the biosphere. They enter the body through water and food and spread through the circulatory system, causing acute toxic reactions [5]. Excessive concentrations of metal ions can have toxic effects on the body. Ba and strontium (Sr) have properties similar to calcium (Ca), a valuable macronutrient for vital processes. These metals can replace Ca, which leads to disruption of the functioning of almost all organ systems. The effect of heavy metals is a threat to health

since they do not degrade biologically and remain in nature and the human body for a long time. Heavy metals have many targets of exposure. They can bind to enzymes, inhibiting their activity, and damage DNA, leading to mutations [6].

In recent years, experimental and epidemiological data have accumulated globally confirming the negative effect of many metal ions during pregnancy [7]. In this work, the focus was directed to alkaline earth metals (Ba and Sr) and heavy metals, such as arsenic (As), thorium (Th), and uranium (U). Studies show that high concentrations of these metals in maternal blood correlate with severe congenital diseases in children [8]. Theoretically, this can happen because the placenta of the embryo is embedded in the maternal circulatory system and transmits toxic substances from the mother to the fetus. The relationship with the complications of pregnancy is also observed [9].

The issue of environmental pollution in Kazakhstan remains unresolved. To prevent negative health consequences, it is necessary to control the quality of food and water consumed by pregnant women. Although some researchers report the negative effects of food processing methods, several studies demonstrate the effectiveness of metal removal technologies. Several papers propose protocols and reagents for removing significant amounts of toxic elements from various types of food [10]. This highlights the importance of an integrated approach to solving the issue of pollution.

A significant amount of research investigates the effects of cooking and processing methods on toxic elements in food. Some studies report a significant decrease in the content of heavy metals in food after cooking, while others indicate an increase in their concentration.

A more effective method of reducing metals in food is the use of chelating compounds: acidic and alkaline solutions, alcoholic solutions when heated, cysteine and homocysteine, organic sulfur-containing complexing agents, ascorbic acid, pectin solutions, dry crushed shells, and the combined effect of alkaline and acidic solutions with reagents for leaching metals (ethylenediaminetetraacetic acid (EDTA), salt, and cysteine) [10].

The study aimed to assess the concentrations of chemical elements, such as Ba, Sr, As, Th, and U, in the biological tissues (placenta and umbilical cord blood) of pregnant women and identify the risks associated with them.

## 2. METHODS

### 2.1 Research design



Figure 1. Study area

The study focused on the analysis of Ba, Sr, As, Th, and U concentrations in the biological tissues (placenta and umbilical cord blood) of women living in the Akmola region of Kazakhstan.

The study was conducted in 2018-2021. Samples were taken from pregnant women living in different districts of the Akmola region (Figure 1).

### 2.2 Study participants

67 pregnant women were selected for the study. In every region, women were selected via computerized random number generation.

The material was taken from the placenta and umbilical blood of the fetuses from 67 women in labor. 48 blood samples were taken from the veins of residents of the following districts of the Akmola region with different ecological situations: Korgalzhyn (Korgalzhyn district), Makinsk and Korgalzhyn (Bulandy district), and Zerendi (Zerendi district). The results of the study will be significant and useful for the authorities, policy makers and health workers of the region, but can't be fully generalized to other regions because of the different industrial and environmental contexts.

The sampling was carried out in the maternity ward of the Kokshetau Perinatal Center, Akmola region. The Bioethics Committee of the Kokshetau Higher Medical College approved the use of the research materials.

Each sample was accompanied by filling out a short questionnaire (No. 1) consisting of 17 questions during childbirth and collecting biomaterial from the studied mother. The questionnaire contains the following information:

1. Full name and age.
2. Place and time of residence.
3. Pregnancy status (the number of pregnancies and how they ended), diseases, complications during the current pregnancy, and the time of their occurrence.
4. Profession and occupational hazards.
5. Obstetric and gynecological, social, and infectious history. An aggravated obstetric history implies one or more abortions, undeveloped or ectopic pregnancy, spontaneous and/or artificial miscarriage, antenatal, intranatal, or neonatal fetal death, or congenital malformations of the fetus or newborn.
6. Gynecological history is characterized by any diseases of the female reproductive organs (cervix, uterus, endometrium, fallopian tubes, ovaries, breast, and congenital malformations).
7. Aggravated infectious history includes any acute infectious pathology that occurred during pregnancy, childbirth, and the postpartum period (COVID-19, tuberculosis, syphilis, hepatitis, acute respiratory viral infection, etc.), exacerbations of chronic foci of infection, or sexually transmitted infections and HIV infection.
8. Aggravated somatic history (extragenital diseases before pregnancy, their exacerbation or decompensation during pregnancy, childbirth, or the postpartum period, including diseases of the cardiovascular system, central nervous system, respiratory system, gastrointestinal tract, allergic diseases, endocrine pathology, etc.).
9. Aggravated social history: alcohol and drug addiction, tobacco smoking and nicotine intoxication, and other types of substance abuse and occupational hazards. Some factors of the labor process and the production environment have an adverse effect on the course of pregnancy. (Reproductive xenobiotics

include medicines, household chemicals, and beauty products).

10. Complications of the current pregnancy.
11. Period of pregnancy.
12. Nature of delivery (spontaneous or operative).
13. Duration of labor and time between membrane rupture and delivery.
14. Complications arising during childbirth.
15. Condition of the newborn (height, weight, Apgar score, congenital malformations).
16. Color of the amniotic fluid and the characteristics of the placenta.
17. Obstetric diagnosis (gestation period, peculiarities of childbirth, weight, height, and Apgar score).

### 2.3 Collecting research material

The biopsy was taken from the central and marginal parts of the placenta and put into separate plastic bags with a clasp. The bags were labeled in sequential numbering with a mark in the questionnaire; the central part was marked with the letter "a", and the marginal part with the letter "b", (e.g.: 1a; 1b; ... 9a; 9b.). Blood from the umbilical cord was collected in special 30-40 ml containers with a lid, the labeling number corresponded to the number of the submitted biopsy material with the letter "k", (e.g.: 1k; 2k; ... 9k).

The collected material was delivered to the laboratory of the Sh. Ualikhanov Kokshetau State University, where biopsy specimens were weighed and ignited in a muffle furnace.

The biopsy was ignited in the following mode: 1 hour at 100°C, then gradually increasing the temperature in the muffle furnace to 600°C.

The material was ignited until it became a constant homogeneous mass (white ash).

The blood was dried at a temperature of 100°C to a dry state.

Before and after ignition, all samples were weighed in porcelain crucibles, after which the finished materials were packed in separate labeled polyethylene bags with a fastener corresponding to the labeling according to ordinal numbering with a mark in the questionnaire: the central part with the letter "a", the marginal part with the letter "b", and blood from the umbilical cord with the letter "k", (1a; 1b; 1k; ... 9a; 9b; 9k).

### 2.4 Research methods

#### 2.4.1 Neutron activation method

The concentration of chemical elements in the blood and placenta was studied using instrumental neutron activation analysis (INAA) using the IRT-T TPU research nuclear reactor (certificate of accreditation No. RA.RU.21AB27 (08.04.2015); analysts: Yu.F. Sudyko, L.F. Bogutskaya). Samples were irradiated with neutrons in a research reactor, resulting in the formation of radioactive isotopes. The gamma radiation emitted by these isotopes was measured to identify and quantify the elements present.

#### 2.4.2 Scanning electron microscope (SEM) method

The samples were studied using a Hitachi S-3400N SEM with a Bruker X@Flash 5010 energy dispersion spectrometer, which allows semi-quantitative elemental analysis with a spatial resolution of a few micrometers. The equipment is located in the Uranium Geology International Innovation Research and Education Center at the Department of Geology of the Engineering School of Natural Resources of the

National Research Tomsk Polytechnical University.

#### 2.4.3 Visual inspection

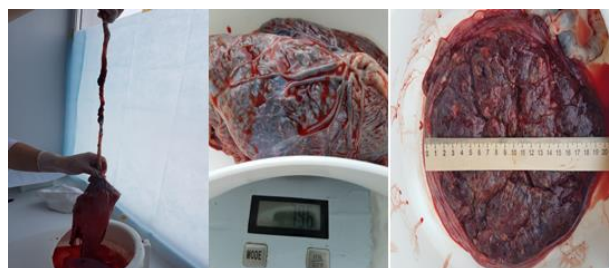
The placenta was carefully visually examined in the workroom for the following: placental tissue and membranes for individual characteristics and pathological changes. The placenta was also measured (with the determination of its diameter and thickness) with a centimeter tape and weighed. These results of the examination were compared to standard references to identify deviations associated with pathological conditions.

When visually examining the structures of the afterbirth, we paid attention to the appearance and color of the fetal membranes and pathological changes in the amnion and umbilical cord.

The data was processed using Microsoft Excel and STATISTICA 64 software [5]. When carrying out the sociological survey and biomedical research, at the meeting dated 24.06.2019, the commission decided to approve and allow the collection of materials for this work. The participants in the study were informed about the progress of the research work and provided consent to participate.

### 3. RESULTS AND DISCUSSION

In our study, placentas with pathological changes were visually common (extensive erosion zones and solid calcinates occupied large areas in the placenta) (Figure 2).



**Figure 2.** Results of the examination of the placenta

When visually examining the structures of the afterbirth, we paid attention to the appearance and color of the fetal membranes and pathological changes in the amnion and umbilical cord. Visual examination is still a widely used method in scientific studies for its practical advantages. Visual assessment offers immediate insights into pathological changes [6].

In all districts, cases of loss of the shiny appearance inherent in the amnion and dissection of the membranes were equally likely. We also observed false knots on the umbilical cord and multiple calcifications in the placenta, increasing its volume and mass (normally 500-600 g). This means that the adaptive and compensatory capabilities of the placenta are connected, increasing in size and leading to hyperplasia.

A visual examination of the placentas of women diagnosed with anemia showed the presence of villus necrosis in the form of infarctions [7].

Malperfusion was also found in the placenta, i.e., abnormal blood vessels in a new mother with a diagnosis of gestational hypertension and mild preeclampsia.

Even with a history and diagnosis of infectious pathologies (e.g., pyelonephritis, chronic viral infection), the development of gestational complications in the form of gestational

toxicosis and anemia, the compensatory capabilities of the placenta are significant. The weight of the fetus during full-term pregnancy is not always affected, but most often remains within the normal range. This is also supported by other research results [8].

The umbilical cord has two arteries and one vein. The length of the umbilical cord is normally 50-62 cm, but the most accurate measurement is carried out in the delivery room (when the fetus is separated from the mother, immediately after childbirth, the length of the umbilical cord decreases by 7-10 cm).

The umbilical cord is considered short when the length is less than 32 cm; this was not observed during this study.

The umbilical cord is considered long when its length is more than 64 cm (three cases), and absolutely long with a length of 72 cm (one case with double entwining of the umbilical cord around the baby's neck). False knots on the umbilical cord were observed in four cases. Varicose veins of the umbilical cord were observed in three cases, with a history of gestational hypertension and mild preeclampsia, of which one patient had calcification of the walls of the umbilical cord vessels.

Thrombosis and calcinates in the umbilical cord wall were observed in one case (in a woman smoking up to 3-5 cigarettes per day during pregnancy). This indicates a prolonged disruption of blood flow in the "mother-placenta-fetus" system.

The fetal membranes were mostly normal when examined (translucent, thin, gray to pink in color).

16 women had cloudy membranes with no physiological transparency and a history of infections. Eight women with meconium imbibition had brown and greenish membrane color.

At the next stage, we evaluated the Ba, As, Th, Sr, and U content in fetal blood (Figure 2) from 28 studied chemical elements. For these elements, the placentas are less barrier-like, and in umbilical cord blood, these elements were found in the same content or higher than in the placenta.

Ba belongs to the essential toxic micronutrients (MNs). In the Korgalzhyn and Bulandy districts, we noted this element in the placental tissue. Women with a pathological course of pregnancy complained about excessive salivation and vomiting in the first half of pregnancy and experienced hypertensive syndrome and preeclampsia in the second half. Additionally, Ba could negatively impact fetal development by inhibiting cell growth and differentiation, leading to developmental defects and abnormal organogenesis [9].

Sr mainly accumulates in bones, can disrupt bone tissue due to the displacement of Ca, and affects the bone marrow and the hematopoiesis system. It also may affect the endocrine system and cause problems with calcium-regulated hormones [10, 11]. As a result, anemia develops, which we observed in 80% of women. Figure 3 shows that the element is contained in the same amount in the placenta and the umbilical cord blood. It can pass through the placenta during the entire period of pregnancy.

Th is a radioactive element. It dramatically increases the risk of pancreatic and blood cancer, but Th ions are necessary for metabolism in combination with other elements, for example, sodium (Na), potassium (K), selenium (Se), and iodine (I). The study showed a Th deficiency. Long-term exposure to Th and external interactions with other elements may increase the risk of congenital malformations such as those of the heart and brain [12].

U is a radioactive and toxic element. Its compounds and nanoparticles often accumulate in the liver, lungs, and kidneys, disrupting DNA and massively killing internal cells. The analysis showed that U was present in the biological substrates of the inhabitants of the districts. U was contained in the same amount in the blood and placenta samples from the Akmla region (Figure 4).

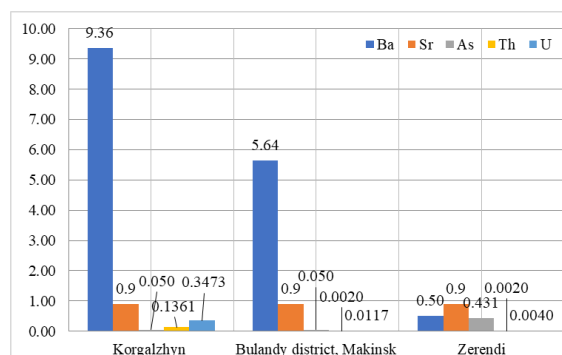


Figure 3. The content of chemical elements in fetal umbilical cord blood

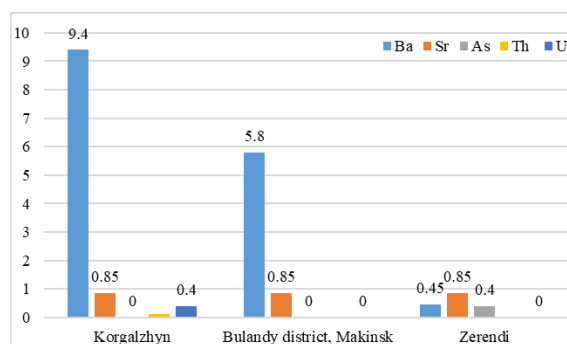


Figure 4. The content of chemical elements in the placenta

For most people, some vital MNs are in short supply, and toxic MNs are in excess due to environmental pollution, poor food quality, depression, and frequent emotional stress.

MNs are part of vitamins and enzymes. Therefore, deviations of the MN effects cannot be considered in isolation from the actions of the latter. The female body during pregnancy needs more vitamins and MNs, and a lack or excess of them damages the health of both the mother and fetus. The risk of perinatal pathology and mortality increases. MN imbalance is often the cause of premature labor, congenital deformities, and disorders of the physical and mental development of children. The lack of vitamins, which include MNs, contributes to the occurrence and development of iron deficiency anemia since the provision of vitamins C and B2 affects the absorption and transport of iron in the body. Folic acid and vitamin B12 are involved in heme synthesis, and vitamin B6 is involved in the maturation of red blood cells [13].

Table 1 shows significant variability in the concentration of Ba, Sr, As, Tb, and U in the placenta. The data demonstrate that Ba and Sr have the highest average concentrations, linked to local environmental conditions, such as industrial emissions. The high variability (V%) of Ba and Sr concentrations suggests that these elements' exposure levels fluctuate significantly across the population. As and U show lower concentrations but are still present, indicating environmental contamination.

**Table 1.** Statistical indicators of the content of chemical elements in the placenta (mg/kg)

Element	M	$\sigma$	S	Xmed	Xmo	min	Max	V (%)
Ba	48.62789	4.282999	40.63	40.63	29.36276	14.70406	139.829	243.90
Sr	0.599121	0.164361	0.05	0.5	1.1268	0.05	5.632749	230.94
As	0.021201	0.005312	0.002727	0.002	0.036414	0.00132	0.178	217.53
Tb	0.337103	0.17042	0.0006	0.0006	1.168341	0.0006	7.770505	190.42
U	0.274712	0.061418	0.0921	0.004	0.42061	0.004	2.464043	164.5

Note: M is the mean.  $\sigma$  is the standard error of the mean. Xmed is the median, and Xmo is the mode. S is the standard deviation. min is the minimum. max is the maximum. V is the coefficient of variation.

**Table 2.** Statistical indicators of the content of chemical elements in the blood

Element	M	$\sigma$	S	Xmed	Xmo	min	Max	V (%)
Ba	14.219	4.877	33.43	5.800	0.5	0.5	210.5	235.1
Sr	11.264	3.654	25.05	0.900	0.9	0.9	94.92	222.3
As	0.645	0.227	1.56	0.050	0.05	0.03	8.037	241.7
Tb	0.011	0.004	0.02	0.001	0.001	0.001	0.105	152.7
U	0.163	8,880.532	60,881.86	0.064	0.0004	0.0002	1.237	78

Note: M is the mean.  $\sigma$  is the standard error of the mean. Xmed is the median, and Xmo is the mode. S is the standard deviation. min is the minimum. max is the maximum. V is the coefficient of variation.

In the blood samples (Table 2), Ba again shows the highest average concentration, with significant variation across individuals. Sr and As are also present, with considerable variability in their concentrations. U is present in small quantities, but the high variability indicates differing exposure levels among the population. These findings suggest that the blood levels of these elements are influenced by environmental factors related to industrial activity and pollution in the region.

An increased concentration of metals in the blood during pregnancy may affect the development of serious health problems, such as preeclampsia. Nowadays, this disease affects about 5-1% of the pregnant women population in the world and could cause neonatal and maternal mortality and even morbidity [14]. It is characterized by high blood pressure after the 20th week of pregnancy, associated with the deterioration of the cardiovascular system [15]. The relationship between environmental pollution and preeclampsia was analyzed using the example of Sr and As.

Stable pollution of the environment with Sr mainly occurs as a result of weathering processes or water erosion of ores rich in Sr and parent rocks in nature. Human activity accelerates this process, leading to the leaching of Sr from the bound state and its entry into the human body through the food chain [16].

Due to the similar chemical properties of Sr and Ca, a high content of Sr in the diet can negatively affect the absorption of Ca by bones and teeth. The average Sr level in the blood serum of pregnant women with early preeclampsia was  $40.9 \pm 13.9$   $\mu\text{g/l}$  and significantly exceeded the Sr level in the control groups ( $30.5 \pm 9.4$   $\mu\text{g/l}$ ). The Ca concentration was significantly lower in women with diagnosed preeclampsia compared to healthy women. Together with a high concentration of Sr, an increase in uric acid and lipid peroxidation was shown, based on which we suggest the participation of Sr in oxidative stress. The exact physio-pathological mechanisms have not yet been identified [17, 18].

It enters the biosphere from geochemical sources and, to a lesser extent, from anthropogenic sources, such as herbicides, growth promoters of farm animals, wood preservatives, the semiconductor industry, etc. [19]. After entry into the body, SAM is modified by one or two methyl groups. A group of

researchers found low concentrations of the dimethyl form of As and high concentrations of inorganic as the blood pressure of pregnant women living in Wuhan [20]. In another cohort of pregnant women in China, concentrations exceeding 15  $\mu\text{g/l}$  were associated with severe preeclampsia [21].

Metals penetrating the placenta negatively affect the developing body, which can lead to stunted growth retardation, disorders in the development of organs and systems, and neurological disorders. High metal levels are associated with an increased risk of congenital abnormalities, such as heart defects and neural tube defects [22].

Two Ba compounds are found in underground sediments: Ba sulfate ( $\text{BaSO}_4$ ) and Ba carbonate ( $\text{BaCO}_3$ ), which enter the environment through natural erosion. However, Ba and its compounds are used in many industrial processes, accelerating erosion and leading to contamination and accumulation in the human body. In the body, Ba stops the cardiac transit current of  $\text{K}^+$  outward, altering the electrophysiological properties of the heart, including membrane depolarization and spontaneous electrical activity. Exposure to Ba can cause a wide range of adverse effects on human health, such as kaliopenia and cardiac arrhythmia. Animal studies show that high levels of Ba in the blood can lead to abnormal ovarian morphology, spontaneous abortions, fetal growth restrictions, and neonatal death. It has also been reported that exposure of the mother to Ba during pregnancy is associated with an increased risk of congenital heart defects [23].

Th and U are the most common naturally occurring radioactive elements in the Earth's crust. Th is usually found in the rare earth mineral monazite, the extraction and processing of which inevitably leads to environmental pollution with Th. U is also an admixture of many minerals. It is assumed that people living near the areas of extraction of raw materials may be exposed to a higher level than those who live far from mining areas [24]. In areas with high levels of radioactive elements, the health of pregnant women and their children is also monitored. Intrauterine exposure to U increases the risk of developing orofacial clefts [25]. Studies of Th toxicity conducted in coal mining and burning sites show that such environmental conditions contribute to the risk of neural tube defects mediated by high Th concentrations [26].

#### 4. CONCLUSIONS

The authors conclude that there are significant health risks for pregnant women living in industrial areas of Kazakhstan. The distribution of the studied elements varied in the "mother-blood-placenta" system. The placenta selectively allows the transport of the MNs and heavy metals to the developing fetus. The placental barrier blocks the transport of toxic xenobiotic metals to the fetus. The demand for macronutrients and MNs varies during pregnancy, and any imbalance between them can cause obstetric pathology. However, an excess of macronutrients, MNs, and vitamins can play a detrimental role in fertility.

Interactions between the elements can affect the homeostasis of the mother and fetus, leading to unexpected biological effects. The data on the content of individual chemical elements indicate that their concentration is influenced by a range of factors of the external environment and internal nature, the study of which is relevant in light of the development of ideas about the health of women and newborns.

Despite Kazakhstan's evolving environmental policy, it is important to note that stricter standards for assessing air, water, and soil quality need to be introduced in industrial regions to reduce the impact of industrial emissions on vulnerable groups, such as pregnant women and newborns.

The main limitations are the relatively small sample size and the lack of a longitudinal study on the health of the children born. Future studies should consider longer-term pregnancy monitoring and assessment of the postpartum health of the women and their children.

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