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ENVIRONMENTAL POLLUTION BY XENOBIOTICS AS A RISK FACTOR FOR THE DEVELOPMENT OF REPRODUCTIVE COMPLICATIONS IN THE POPULATION OF THE INDUSTRIAL REGION

T.A. Holovkova

Dnipro State Medical University, Dnipro, Ukraine

e-mail: tgolovkova@i.ua

T.A. Holovkova ORCID: <https://orcid.org/0000-0002-0379-3398>

In the conditions of deterioration of the population's health and the demographic situation as a whole the problem of the chronic impact of environmental factors on the human body, especially sensitive sections of the population, requires comprehensive and effective actions from the public health system to minimize the negative impact of xenobiotics on the environment, among which heavy metals occupy an important place, and stimulates the search for special scientific developments in the field of preventive medicine.

The purpose of the work. *Determination of the influence of heavy metals on the frequency and prevalence of reproductive complications of pregnancy and childbirth among residents of the Dnipropetrovsk region.*

Materials and methods. *On the basis of studies of the content of lead and cadmium in the air, drinking water and food products of the 2 industrial districts of Dnipro and in the city of the comparison - Novomoskovsk during 10 years, the estimation of the complex flow of heavy metals to the organism of the inhabitants of the cities of observation was carried out.*

The degree of the influence of the heavy metals of the environment on the state of the reproductive health in the population was analyzed by epidemiological retrospective studies analysis of data from primary statistical documentation on complications of pregnancy and childbirth. Mathematical processing of the results consisted of calculating primary statistical indicators, identifying their differences, determining the relationship between variables using parametric and non-parametric correlation analysis, and calculating the relative risk of reproductive complications as an integral part of the observations of the occurrence of reproductive complications.

Results. *The obtained results show that heavy metals are constantly determined in the environmental objects of the industrial areas. Biomonitoring data confirm assumptions about the technogenic loading of pregnant women's organism with toxicants in industrially populated cities, which poses a potential risk of adaptation failure for this critical group of residents of Dnipro, even at relatively low xenobiotic concentrations.*

Conclusions. *It was established the increase in the metal-toxicant load of the organism of women of the industrial city compared to the control one, which is accompanied not only by a significantly higher frequency of reproductive complications but also correlated with the lead and cadmium content in the environmental objects of the residential area.*

The above indicates that there is a statistical probability of the development of the complications of pregnancy and childbirth in women under the influence of abiogenic metals of the environment, which is 2.8-3.2 times higher for women in industrial areas than for pregnant women in control city, except for the weakness of labor activity ($R < 1$).

Keywords. *Heavy metals, xenobiotics, environmental pollution, exposure, pregnant women, biosubstrates, public health, reproductive complications, man-made polluted areas.*

ЗАБРУДНЕННЯ ДОВКІЛЛЯ КСЕНОБІОТИКАМИ ЯК ФАКТОР РИЗИКУ РОЗВИТКУ РЕПРОДУКТИВНИХ УСКЛАДНЕНЬ У НАСЕЛЕННЯ ПРОМИСЛОВОГО РЕГІОНУ

Головкова Т.А.

Дніпровський державний медичний університет, м. Дніпро, Україна

В умовах погіршення здоров'я населення та демографічної ситуації у цілому проблема хронічного впливу екологічних чинників на організм людини, особливо чутливих її верств населення, потребує від системи громадського здоров'я комплексних та ефективних дій з мінімізації негативного впливу ксенобіотиків довкілля, серед яких вагоме місце посідають важкі метали, та стимулює пошук спеціальних наукових розробок в галузі профілактичної медицини.

Мета. *Визначення впливу важких металів на частоту та поширеність репродуктивних ускладнень вагітності та пологів у мешканок Дніпропетровської області.*

Матеріали і методи досліджень. *На основі досліджень вмісту свинцю і кадмію у повітрі, питній воді та харчових продуктах двох промислових районів міста Дніпро та міста порівняння – Новомосковська протягом 10 років, здійснено оцінку комплексного надходження важких металів в організм мешканців міст спостереження.*

Виконані епідеміологічні дослідження шляхом ретроспективного аналізу даних первинної статистичної документації щодо ускладнень вагітності і пологів. Математична обробка результатів складалась з розрахунку первинних статистичних показників, виявлення їх відмінностей, визначення взаємозв'язку між змінними за допомогою параметричного та непараметричного кореляційного аналізу та розрахунку відносного ризику виникнення репродуктивних ускладнень під впливом важких металів навколишнього середовища.

Результати дослідження та їх обговорення. *Отримані результати показали, що важкі метали постійно визначаються в об'єктах промислових районів міста. Дані біомоніторингу підтверджують припущення про техногенне навантаження організму вагітних токсикантами в промислово розвинутих районах, що створює потенційний ризик збою адаптації для цієї критичної групи жителів Дніпра, навіть при відносно низьких концентраціях ксенобіотиків.*

Висновки. *Встановлено підвищення металотоксичного навантаження на організм жінок промислового міста, порівняно з контрольним, що супроводжується не тільки значно більшою частотою репродуктивних ускладнень, але й корелює з вмістом свинцю та кадмію в об'єктах навколишнього середовища житлової зони. Вищезначене свідчить про статистичну ймовірність розвитку ускладнень вагітності та пологів у жінок під впливом абіогенних металів зовнішнього середовища, яка у жінок промислових районів у 2,8-3,15 рази вище, ніж у вагітних контрольного міста, за винятком слабкості родової діяльності ($R < 1$).*

Ключові слова. *Важкі метали, ксенобіотики, забруднення довкілля, вплив, вагітні жінки, біосубстрати, громадське здоров'я, репродуктивні ускладнення, техногенно забруднені території.*

The Concept of the National Program "Health 2020: The Ukrainian Dimension" states that in recent times there has been an unfavorable medical and demographic situation in Ukraine, it indicates the poor health of the population and the prevalence of chronic noncommunicable diseases [1]. The results of scientific researches give grounds to claim that the inhabitants of urbanized territories have ecologically conditioned diseases, under the negative influence of the harmful environment of human existence [2,3], which is connected with the intensity of environmental factors that go beyond biological adaptation and create a direct threat to life [4].

From the point of view of hygienic importance of the wide variety of harmful environmental factors causing women's health disorders, chemical compounds occupy a priority place, among

which are the attention of sufficiently widespread contaminants from the group of heavy metals (HMs) due to the fact that their impact on the human body determines the variety of pathogenetic mechanisms and their accuracy in the generative function [5,6]. One of the clinical manifestations of lead toxicity is anemia, the development of which is associated with impaired heme biosynthesis and accelerated erythrocyte destruction. Cadmium blocks the work of a number of enzymes important for life, in addition, it is capable of damaging the liver, kidneys, and lungs, and in the last months of pregnancy, a significant content of cadmium in the body may be the cause of pregnancy gestosis [3,4]. The negative effect of toxic metals on critical population groups is manifested not only in connection with the increase in the intensity of influence, but also in the reduction of adaptation reserve, including during pregnancy, which changes the reactivity of the organism and can serve as a trigger mechanism of the damaging effect of xenobiotics [7,8].

In an unstable demographic situation, the problem of chronic environmental impact on the female body and offspring stimulates the emergence of special sections in related medical sciences to seek scientific developments in the field of preventive medicine. Also, limited data that would reveal the mechanisms of adverse effects of small doses of HMs are needed to develop effective means of preventing ecological dependent pathology, including reproductive complications [9].

The aim of the work was to determine the impact of technologically contaminated environment with lead and cadmium on the reproductive complication rates in pregnant women - residents of Dnipropetrovsk region.

Materials and methods. The industrial districts of the Dnipro, such as Industrial and Novokodatsky, corresponded to the goals and objectives of the study to the greatest extent. Despite the location in one city, the study areas differ in the nature and intensity of atmospheric air pollution, the water supply system, the relief, and so on. A large number of industrial sites are located on their territory, with residential areas close to the sanitary protection zones of enterprises and characterized by heavy traffic. The city of Novomoskovsk (26 km away from the city of Dnipro) was chosen as the control area, which most closely meets the requirements of contrast: it contains a small number of industrial objects, the volume of solid emissions into the air is 10 times lower than in the city of Dnipro [4]. These studies have been performed according to the Declaration of Helsinki, and the procedures have been approved by the Commission on Biomedical Ethics of Dnipro State Medical University (protocol No. 1 dated 15.01.2020), which concluded that the work met generally accepted moral standards, requirements for rights, interests and personal dignity of the studied participant.

In the first phase of the program, systematic sampling of air, drinking water and food was carried out in the residential areas of the observation areas. The content of lead and cadmium was determined by the atomic absorption method [10], because it is characterized by high accuracy, sensitivity and allows to determine many elements simultaneously. Hygienic assessment of the obtained concentrations was carried out in accordance with the requirements of generally accepted normative documents. The next step was the biomonitoring of metals, which considers the method of determining the degree of danger of environmental factors and is necessary for hygienic studies [11]. When determining the content of toxicants in the blood and urine of pregnant women, women were divided into three groups by place of residence: women from Dnipro (respectively Industrial and Novokodatsky districts) were included into groups I and II, and control group - residents of Novomoskovsk. For the examination, 89 practically healthy women aged 20-25 years were selected, without occupational harm, in the absence of somatic, hereditary diseases and harmful habits, with a physiologically normal course of pregnancy of the second trimester. Subsequently, epidemiological studies were performed by retrospective analysis of data from primary statistical documentation on complications of pregnancy and childbirth. Observational groups are formed by homogeneous homogeneous conditions, lack of somatic pathology and weighted heredity, bad habits and occupational harms. Out of the variety of reproductive complications, 15 were selected for further statistical analysis, the manifestations of which are most associated with the negative impact of the environmental HMs [5,12]. The extent of the environmental impact of HMs on reproductive health status in residents of anthropogenically

contaminated territories has been analyzed by assessing the relative risk of reproductive complications as an integral part of hygienic and epidemiological surveillance. The obtained data were processed by traditional methods of variational statistics, using licensed statistical software packages of Statistica v.6.1 (Statsoft Inc., USA, license number AJAR909E415822FA).

Results. The results of the studies show that in the atmospheric air of the Novokodatskyi district lead is registered in 91,7% of samples, cadmium in 59%, in the air of the Industrial district – 100% and 75% respectively, whereas the presence of these metals in the drinking water of both industrial of the districts is 100%. In the drinking water supplied by the Industrial District, the average monthly concentration of lead sometimes reached the upper limit of the standard – 0,01mg/dm³ [4]. In the control city, xenobiotics in air and drinking water samples were determined periodically, with statistically significant lower content than in the Dnipro districts. Dnipro food products contain toxicant metals in concentrations not exceeding the respective maximum permissible concentrations (MPC), with the exception of lead content in food fats, which is 0,12 mg/kg at MPC 0,1 mg/kg [13]. The analysis of lead and cadmium content in Novomoskovsk products under study shows that the concentrations of these metals do not have significant differences with those of Dnipro, except for the group of food fats.

Analysis of biomonitoring data from three groups of women (table 1) indicates that women's lead concentrations range from 0,11 µg/ml to 0,77 µg/ml. For the surveyed group I, the average value of lead in the blood is 0,35±0,027 mg/ml, which is statistically significantly higher than in the women of II (p<0,05) and III group (p<0,01) – 0,27±0,017 µg/ml and 0,18±0,007 µg/ml, respectively. On average, lead content in the blood of pregnant women in group II is 33% higher than in women in group III, which is statistically significantly confirmed (p<0,01).

Table 1. Average concentrations of heavy metals in the blood and urine of pregnant women - residents of Dnipro (I – Industrial district, II – Novokodatskyi district) and Novomoskovsk (III control district) (M±m).

Concentration of metals in the biosubstrates, µg/ml	Observation groups			Physiological limits of norm		
	I (n=33)	II (n=30)	III (n=26)	standard	metal carrier	intoxication
Blood						
lead	0,35±0,027*, ***	0,27±0,017**	0,18±0,007	0,2	0,2-0,4	> 0,4
cadmium	0,062±0,004***	0,092±0,006**	0,028±0,002	0,02	0,02-0,3	> 0,3
Urine						
lead	0,043±0,004***	0,038±0,002**	0,025±0,002	-	-	0,4
cadmium	0,079±0,01***	0,089±0,006**	0,034±0,004	-	-	0,08

Note: * – significant differences between groups I-II (p<0,05), ** – significant differences between groups II-III (p<0,01), *** – significant differences between groups I-III (p<0,01).

Urine of the tested women contains lead at concentrations ranging from 0,01 to 0,103 µg/ml. The average values of lead in urine are: 0,043±0,004 µg/ml for group I, 0,038±0,002 µg/ml for group II, 0,025±0,002 µg/ml for group III. In both the blood and urine, the average lead content in the surveyed industrial districts is 1,3 and 1,13 times higher than for women in the Novokodatskyi district, and by almost 2 and 1,72 times, respectively, compared to Novomoskovsk.

The level of cadmium in the blood of women ranges from 0,01 to 0,17 µg/ml. This value in women of group I averages 0,062±0,004 mg/ml, which is significantly (p<0,01) lower than in pregnant women of group II – 0,092±0,006 mg/ml. The content of cadmium in the blood of the control group is 0,028±0,002 µg/ml, which is significantly lower (p<0,01) than in Dnipro women.

The average concentration of cadmium in the urine of pregnant women of group I was 0,079±0,01 µg/ml, for group II – 0,089±0,006 µg /ml. In the control group, the concentration of cadmium in the urine averages 0,034±0,004 µg/ml, which significantly (p<0,01) lower than in

Dnipro women. In addition, in 36% of women in group I, in 50% of women in group II, the content of cadmium in urine is higher than the norm. In the control group, only 7,7% of pregnant women demonstrated the increased values of the toxicant content in urine. Thus, its average concentrations in the blood of pregnant women of group II exceed the data for women of the Industrial region by 1,5 times, in urine - by 0,01 $\mu\text{g/ml}$, and, in comparison with the city of Novomoskovsk, the average value of cadmium in the blood is higher by 3,3 times, and in urine – 2,6 times.

The results of the analysis of epidemiological studies show the frequency of complications of pregnancy and childbirth in women of the Industrial area was 141,6%, Novokodatskyi – 133,6%, respectively, while women of the control city of Novomoskovsk these figures make 92,4%. It is also established that in practically healthy pregnant women from the investigated complications of pregnancy are most often reported anemia I and II half of pregnancy (9,5-17,2% and 18,3-26,7%), preeclampsia (18,7-27,3%), threatening abortion and premature labor (12,5-24,3% and 8,2-15,6%). It should be noted that the highest incidence of most complications is statistically significantly higher by 3,1-11,8% in women in Dnipro industrial areas compared to the control ($p < 0,05$). With regard to the studied complications of childbirth of pregnant women, labor and delivery complicated by pathologic states of umbilical cord and premature rupture of membranes. Thus, for women of the Industrial district this value is respectively $11,7 \pm 1,3$ and $10,6 \pm 0,6\%$, Novokodatskyi – $12,1 \pm 2,0$ and $9,5 \pm 0,8\%$, Novomoskovsk – $10,1 \pm 1,5$ and $9,4 \pm 0,8\%$. Particular attention should be paid to the fact that of all the species studied reproductive complications poor uterine contraction strength ($3,0 \pm 0,3\%$) in the control group recorded significantly more ($p < 0,01$) than observed in industrial areas ($1,7 \pm 0,2\%$ to $1,9 \pm 0,1\%$).

The data obtained provided the basis for correlation analysis in order to establish a correlation between the negative impact of environmental HMs on the frequency of reproductive complications of women living in industrial areas. The coefficients of paired correlation between lead and cadmium contamination of environmental objects and the prevalence rates of gestosis in pregnant women and complications of childbirth demonstrate the existence of relationships.

According to the results of mathematical data processing, there is a reliable relationship between the occurrence of complications such as labor and delivery complicated by pathologic states of umbilical cord ($r = 0,73$; $p < 0,01$), anemia which complicates pregnancy of the other half ($r = 0,61$; $p < 0,05$) and premature labor ($r = 0,65$; $p < 0,05$) and lead content in the air, as well as a tendency for their association with cadmium concentration ($r = 0,51$, $r = 0,49$ and $r = 0,52$, respectively; $p < 0,1$) in the surface atmosphere. The manifestations in women of the frequency of placental disorders tends to be related to the content of cadmium ($r = 0,51$; $p < 0,1$) and lead ($r = 0,46$; $p < 0,1$) in the atmospheric air of the area of residence (Figure 1).

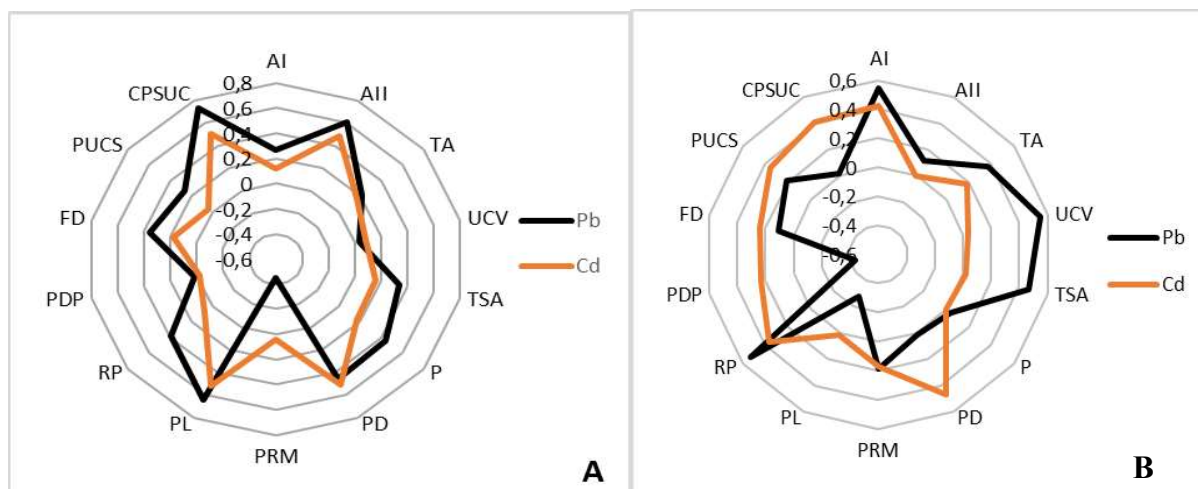


Figure 1. Values of the pair correlation coefficients between the frequency of reproductive complications in women and the concentration of lead and cadmium in the atmospheric air (A) and in drinking water (B) of the studied areas.

Note: values of the pair correlation coefficients between the frequency of reproductive complications in women: anemia which complicates recent pregnancy (A I), anemia which complicates pregnancy of the other half (A II), threatening abortion (TA), uncontrollable vomiting during pregnancy (UCV), threatened spontaneous abortion (TSA), preeclampsia (P), placental disorders (PD), premature rupture of membranes (PRM), premature labor (PL), retention of placenta or membranes (RP), premature detachment of placenta (PDP), fetal distress (FD), poor uterine contraction strength (PUCS), labor and delivery complicated by pathologic states of umbilical cord (CPSUC) and the concentration of lead and cadmium in the atmospheric air and in drinking water of the studied areas.

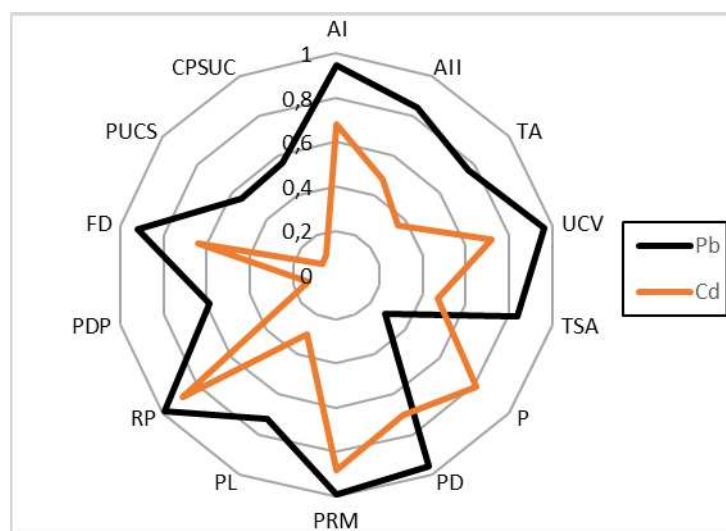


Figure 2. Values of pair correlation coefficients between the frequency of reproductive complications in women and the concentration of lead and cadmium in food in the areas of observation.

Note: values of the pair correlation coefficients between the frequency of reproductive complications in women: anemia which complicates recent pregnancy (A I), anemia which complicates pregnancy of the other half (A II), threatening abortion (TA), uncontrollable vomiting during pregnancy (UCV), threatened spontaneous abortion (TSA), preeclampsia (P), placental disorders (PD), premature rupture of membranes (PRM), premature labor (PL), retention of placenta or membranes (RP), premature detachment of placenta (PDP), fetal distress (FD), poor uterine contraction strength (PUCS), labor and delivery complicated by pathologic states of umbilical cord (CPSUC) and the concentration of lead and cadmium in food of the studied areas.

Of particular interest are the results of the correlation analysis of the frequency of reproductive complications in women in industrial areas and the content of HM in food (Figure 2). In particular, a positive reliable relationship was established between the development of anemia which complicates recent pregnancy, uncontrollable vomiting during pregnancy, placental disorders, premature rupture of membranes, retention of placenta or membranes with lead concentration in food ($r=0,89-0,99$; $p<0,05$). The content of cadmium in the foods is associated with the retention of placenta or membranes ($r=0,89$; $p<0,05$), and the manifestations of preeclampsia and premature rupture of membranes tend to be associated ($r=0,81$ and $r=0,88$, respectively; $p<0,1$) with the concentration of this toxicant in products.

The relative risk of pregnancy and childbirth complications in women in the studied area was calculated to assess the degree of influence of environmental HM on the occurrence of reproductive complications. Analysis of the results of determination of risk, considering the confidence interval, indicates the statistical significance of the development of all studied

complications for pregnant women from the specified risk factor ($R>1$), with the exception of poor uterine contraction strength ($R<1$). The risk of anemia which complicates pregnancy premature labor, uncontrollable vomiting during pregnancy, premature rupture of membranes in women in industrial areas is 2,8 times higher than in pregnant women in Novomoskovsk. In addition, residents of the Industrial District have a tendency to increase the risk of these complications compared to women in the Novokodatskyi district. The course of pregnancy and childbirth in the residents of the Novokodatskyi district tends to increase the risk of preeclampsia, placental disorders, retention of placenta or membranes, premature detachment of placenta, the threat of fetal distress and labor and delivery complicated by pathologic states of umbilical cord in comparison with women of the comparative city.

Discussion. Ecological and hygienic studies have established that heavy metals are constantly detected in air samples, drinking water and food of the studied areas within the MPC. However, in the control town, xenobiotics in the environment was determined periodically, with a statistically significant lower content than in the areas of the city of Dnipro ($p<0,05$ – $p<0,01$) and correlates with literature data [14].

We evaluated peculiarities of HM content in biosubstrates of women, depending on the level of technogenic pollution of the territory of residence. Our data showing, that women's lead concentrations in blood is in agreement with the data [15] in women with physiological pregnancy who live in other industrial cities. Average values of lead content in the blood of pregnant women - residents of industrial and comparative cities do not exceed the physiological norm – 0,4 mg/l [11]. However, in 24% of patients living in Industrial District and 6.7% women living in Novokodatskyi one, there was an increase in blood lead levels relative to the physiological norm. At the same time, in 60% of pregnant women of group I, in 76,6% of group II and in 30% of women of group III, the lead content in blood is determined within the limits of metal - from 0,2 to 0,4 $\mu\text{g/ml}$ [11]. Only 16% of women living in the Industrial District and 16.7% of Novokodatskyi one, blood lead concentrations meet the existing physiological norms, while in Novomoskovsk this figure is much higher and is 70%. Despite the fact that the lead content in the blood of women in the control city is significantly lower than in the inhabitants of the industrial city - by 33,0-48,6% ($p<0,01$), its level exceeds the data for unpolluted territories [15,16].

We revealed that the average values of lead in urine correspond to the norm – 0,04 mg/l [11] except for values for Industrial District residents [4]. We did not reveal an excess of lead in urine in any of the examined control groups of pregnant women, while in 44,8% of pregnant women of group I and 40% of group II this indicator was higher than the normative one, the content of this metal in the urine of women in the comparative city is significantly lower by 34,2-41,9% ($p<0,01$) than in women in industrial areas, by 0,013-0,018 $\mu\text{g/ml}$ what is relevant to literature data [16].

The concentration of cadmium in the blood of women coincides with similar data for man-made areas [15,17] and reliably – 2,2-3,3 times higher than the indicators of women in the control city ($p<0,01$) and does not exceed the normative content – 0,3 $\mu\text{g/ml}$ [11]. But in 96,7% of pregnant Novokodatskyi district, the cadmium concentration in the blood is higher than 0,02 $\mu\text{g/ml}$, which is considered as the limit of metal for this toxicant. In the Industrial District 18% of the surveyed found cadmium in the blood. With regard to concentrations of cadmium in the urine of pregnant women – its average concentration for women of industrial city identified practically at the level of normative value – 0,08 $\mu\text{g/ml}$ [11] – group I, 10% higher than the standard level group II and significantly higher compared to women in the control city ($p<0,01$). In addition, in 36% of women in group I, in 50% of women in group II, the content of cadmium in urine is higher than the norm. In the control group, only 7,7% of pregnant women demonstrated the increased values of the toxicant content in urine. Thus, its average concentrations in the blood of pregnant women of group II exceed the data for women of the Industrial region and in comparison, with the city of Novomoskovsk, the average value of cadmium in the blood is higher by 3,3 times, and in urine – 2,6 times.

Biomonitoring data confirm assumptions about the technogenic loading of pregnant women's environment with toxicants in industrially populated cities, which poses a potential risk of

adaptation failure for this critical group of residents of Dnipro, even at relatively low xenobiotic concentrations [4], which correlates with the results of studies by other authors [6,12]. The reasons for this may be the effect of lead on the reproductive function of women, mainly due to decreased fertility, delayed conception and changes in hormonal levels and blood circulation, which affects pregnancy and its outcome [3,18].

The results of the analysis of epidemiological studies showed that the frequency of complications of pregnancy and childbirth among all women – residents of an industrial city were 45,67-46,68%, which is 12,7-14,6% higher compared to the data of the control city. At the same time, we revealed a frightening situation – according to the results of the examination of pregnant women, the number of women, who had no pregnancy and childbirth complications during the study period in the industrial city it was only 6,0-8,6%, while in the control city it was 19%.

The analysis revealed that the highest overall frequency of complications of pregnancy and childbirth is observed in women of the Industrial area. It is also established that in practically healthy pregnant women – permanent residents of the areas of observation from the investigated complications of pregnancy are most often reported anemia I and II half of pregnancy, preeclampsia, threats of pregnancy termination and premature birth, which is in line with other researchers [3,6] about the most frequent manifestations of these complications in the inhabitants of man-made contaminated territories. It should be emphasized that although these complications have an increased incidence of occurrence in Dnipro women, no statistical evidence of the difference of these values for the observation areas was found.

According to the results of mathematical data processing, we found that there is a reliable relationship between the occurrence of complications such as labor and delivery complicated by pathologic states of umbilical cord, anemia which complicates pregnancy of the other half and premature labor and lead content in the air ($r=0,61-0,73$; $p<0,05$ – $p<0,01$), anemia which complicates recent pregnancy, uncontrollable vomiting during pregnancy, placental disorders, premature rupture of membranes, retention of placenta or membranes with lead concentration in food ($r=0,89-0,99$; $p<0,05$).

Most often, preeclampsia of pregnant women was registered with residents of the Novokodatskyi district and had a significant association with cadmium content in drinking water ($r=0,76$; $p<0,05$). Taking into account the data of biomonitoring of cadmium in the blood of women of group II, whose concentrations were significantly higher by 1,5 and 3,3 times in comparison with the data of the surveyed Industrial district and the control city, it is possible to suppose the adverse effect of cadmium of technogenic origin on the system of adaptation of the organism of women during pregnancy with the subsequent development of preeclampsia.

The manifestations in women of the frequency of placental disorders tends to be related to the content of cadmium ($r=0,51$; $p<0,1$) and lead ($r=0,46$; $p<0,1$) in the atmospheric air of the area. The content of cadmium in the food is associated with the incidence of retention of placenta or membranes ($r=0,89$; $p<0,05$), the manifestations of preeclampsia and premature rupture of membranes ($r=0,81$ and $r=0,88$, respectively; $p<0,1$).

Our data showing that residents of the city of Dnipro are at increased risk of developing all studying complications, except for the poor uterine contraction strength, compared to women of the control city. Women of the Industrial district have an increased risk of complications of pregnancy, and women of the Novokodatskyi district – childbirth.

The established values of the risk of complications during pregnancy and childbirth in women of industrial cities in comparison with the control confirms the negative impact on reproductive health of TM residents of technologically contaminated areas [2,5,19]. Analysis of the results shows a statistical probability of developing complications of pregnancy and childbirth in women under the influence of abiogenic metals of the environment [6], which in industrial women is 2,8-3,2 times higher than in pregnant women in Novomoskovsk, except for weakness patrimonial activity ($R<1$).

Conclusions

1. It was found that heavy metals are constantly present in the life support environmental objects of the industrial city – in the range of 59,0-91,7% of samples for lead and 75-100% of samples for cadmium, but in concentrations not exceeding hygienic standards, although with statistically significant higher content than in the control, relatively clean city.
2. Despite the relative compliance of the content of heavy metals in the environment with hygienic requirements, this situation poses a real threat of internal contamination during pregnancy, as evidenced by high concentrations of lead and cadmium in biosubstrates in women in industrial areas, which in 6,7-44,8% of cases exceed the physiological level in various biosubstrates and the results of studies of pregnant women control city, metal carrier is found in 18,0-96,7% of pregnant women in different industrial areas of the city. The average values of cadmium content in the urine of patients of group II exceeded the permissible concentration by 10% while in 36-50% of women an excess of the normative level of cadmium in urine was revealed.
3. The established increase in metallotoxic load on the body of women in industrial cities, compared with the control, is accompanied not only by a much higher frequency of reproductive complications, but also correlates with lead and cadmium in the environment of industrial cities ($r=0,46$ – $r=0,99$; $p<0,05$ – $p<0,001$) and causes an increase in the relative risk of complications of pregnancy and childbirth in women, which is 2,8-3,2 times higher than in pregnant women in Novomoskovsk, except for the weakness of labor ($R<1$).

Prospects for further research. The results of the study allowed to scientifically substantiate the need for further research to develop and implement effective measures to prevent the negative impact of xenobiotics on the reproductive health of women living in industrialized regions to reduce the man-made load of heavy metals on critical populations, increase compensatory reserves of the body of pregnant and strengthen their health.

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