

UDC 618.3-008.6-06-092:612.014.46:(546.48+546.81)

LEAD AND CADMIUM AS RISK FACTORS FOR DEVELOPMENT OF GESTATIONAL COMPLICATIONS

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Introduction. *Considering intensive chemical environmental pollution, health care is one of the priority problems in modern medicine. Nowadays, heavy metals, particularly lead and cadmium, which are classified as global environmental pollutants, adversely affect public health. Even low concentrations of these metals and their compounds can accumulate and result in decrease of adaptive body reserves. Under such conditions, generative function is among the least protected and most susceptible ones. In this regard, the concept of reproductive health as a sensitive indicator of ecological problem was stated.*

The aim of this study was to evaluate lead and cadmium levels in women's blood in uncomplicated and complicated pregnancy and to assess the significance of their influence on the gestational process.

Materials and methods. *Investigation of lead and cadmium content in the blood of 42 women with uncomplicated pregnancy and 50 women with gestation complicated by anemia (44.0 %) and threatened abortion (56.0 %) was carried out. Determination of metals was evaluated by inversion voltammetry method.*

Results. *An average concentration of lead in the blood of women with uncomplicated gestation corresponds to generally accepted levels. However, in 11.9 % of pregnant women, metal content was detected within 0.2 to 0.4 mg/l, which is rated as "carriage" and in 4.8 % of women, lead concentrations slightly exceeded the upper level of acceptable content (> 0.4 mg/l). Comparing the results with the data of the Center for Disease Control, physiologically acceptable level of lead (0.1 mg/l) was determined in 57.1 % of women with uncomplicated gestation. Exceeding of this level was detected in 42.9 % of pregnant women, which can cause hypertension in adults and leads to lower IQ, hearing, and growth in children. It is disturbing to determine the lead level above 0.45 mg/l in 11.1 % of women, which is too high and without timely medical aid is dangerous for children's health.*

The average level of lead in complicated pregnancy was defined as "alertness" (0,2-0,4 мг/л) and was 2.4 times higher than in women with uncomplicated course of gestation. The highest concentration of metal was recorded in the blood of women with threatened miscarriage, which was by 154.0 % higher than in uncomplicated pregnancy. At the same time, lead level in women with anemia exceeded the index in physiological gestation by 95.2 %. In comparison with the data of the Center for Disease Control (USA), physiologically acceptable level of lead was determined only in 12.0 % of women with complicated gestation. In 88.0 % of women (in anemia – 86.3 %, threatened abortion – 89.2 %), exceeding of the maximal physiologically acceptable level is observed. Among them, in 63.6 % cases lead concentrations ranged within 0.2-0.44 mg/l, which is regarded as being high for children and "alarming" for adults. Potentially harmful level of lead was observed in 25.0 % of women.

The level of cadmium in the blood of the women with physiological pregnancy corresponded to the known options for an average person (< 0.013 mg/l) and was slightly higher than recommended by the American Conference of Governmental Industrial Hygienists (0.005 mg/l). If compared with the approximate reference level of cadmium in the adults' blood, cadmium content was determined within 0.005-0.01 mg/l in 33.4 % of women with uncomplicated gestation, which is estimated as the level of "alertness", and potentially harmful levels were found in 9.5 % of cases (> 0,01 мг/л).

The average level of cadmium during complicated pregnancy exceeded acceptable level 3 times and 2.8 times the index in uncomplicated gestation. In 44.0 % of women, cadmium was determined in "alert" range, potentially harmful level was found in 40.0 %. The highest content of cadmium was recorded in threatened miscarriage which exceeded the index in physiological gestation 3.2 times. However, pregnant women with anemia had 2.4 times higher cadmium level than healthy ones.

Conclusions. *Nowadays in ecological conditions with increased levels of abiotic substances, it is reasonable to implement detection of lead and cadmium contents into practical health care, especially in early gestation, as risk factors for development of gestational complications, which in its turn can protect the health of women and newborns.*

Key words: *pregnancy, lead, cadmium, gestational complications.*

СВИНЕЦЬ ТА КАДМІЙ ЯК ЧИННИКИ РИЗИКУ РОЗВИТКУ ГЕСТАЦІЙНИХ УСКЛАДНЕНЬ

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Вступ. *З урахуванням інтенсивного хімічного забруднення навколишнього середовища проблема збереження здоров'я населення є одним із пріоритетних напрямків сучасної медицини. Сьогодні чималий вплив на стан здоров'я мають важкі метали, зокрема свинець та кадмій, які належать до категорії глобальних забруднювачів довкілля. Навіть у низьких концентраціях ці метали та їх сполуки здатні накопичуватись та призводити до зниження адаптаційних резервів організму. За таких умов однією з найменш захищених і найбільш вразливих є генеративна функція, у зв'язку з чим, було сформульовано концепцію про репродуктивне здоров'я людини як чутливий індикатор екологічного неблагополуччя.*

Мета роботи – дослідження вмісту свинцю та кадмію у крові жінок за неускладненого та ускладненого перебігу вагітності й оцінка значущості їх впливу на перебіг гестаційного процесу.

Матеріали і методи. *Досліджено вміст свинцю та кадмію в крові 42 жінок із неускладненою вагітністю та 50 жінок, в яких перебіг гестації ускладнився анемією (44,0 %) та загрозою переривання вагітності (56,0 %). Визначення металів проводилось методом інверсійної вольтамперометрії.*

Результати. *Середня концентрація свинцю в крові жінок із неускладненою гестацією узгоджується із загальноприйнятими рівнями, однак у 11,9 % вагітних вміст металу визначався в межах від 0,2 до 0,4 мг/л, що оцінюється як «металоносіяство», а в 4,8 % жінок концентрація свинцю дещо перевищувала верхній рівень прийнятного вмісту (> 0,4 мг/л). При порівнянні із даними Центру з контролю за захворюваннями, то у 57,1 % жінок з неускладненою гестацією визначався фізіологічно прийнятний вміст свинцю (до 0,1 мг/л). Перевищення цього рівня виявлено у 42,9 % вагітних жінок, що може спричинити гіпертензію у дорослих та призвести до зниження IQ, слуху, темпів росту у дітей. Викликає занепокоєння визначення рівня свинцю понад 0,45 мг/л у 11,1 % жінок, що вважається дуже високим та без своєчасної медичної допомоги небезпечним для життя дитини.*

Середній рівень свинцю при ускладненій вагітності визначався в «насторожуючих» межах (0,2-0,4 мг/л) й у 2,4 раза перевищував показник при неускладненій гестації. Найвища кон-

центрація металу зафіксована у крові жінок із загрозою викидня, що на 154,0 % більше, ніж при неускладненій вагітності. Водночас у вагітних жінок з анемією рівень свинцю на 95,2 % перевищував показник при фізіологічній гестації. Порівняно з даними США прийнятний рівень свинцю при ускладненій гестації визначався лише у 12,0 % жінок. У 88,0 % жінок з (при анемії у 86,3 %; при загрозі переривання – у 89,2 %) відзначається перевищення максимумально фізіологічно прийнятного рівня. З них у 63,6 % вміст свинцю коливався в межах 0,2-0,44 мг/л, що розцінюється як високий щодо дітей та як «насторожуючий» стосовно дорослого населення. У 25,0 % жінок виявлено потенційно небезпечний вміст свинцю.

Рівень кадмію у крові жінок з фізіологічним перебігом вагітності узгоджується з відомими показниками для умовної людини (до 0,013 мг/л) та незначно перевищує рекомендації американців (0,005 мг/л). При порівнянні з орієнтовними референтними рівнями кадмію у крові дорослого населення, то у 33,4 % жінок з неускладненою гестацією вміст металу визначався в межах 0,005-0,01 мг/л, що оцінюється як рівень «настороженості», а у 9,5 % виявлено потенційно шкідливий рівень (>0,01 мг/л).

Середній рівень кадмію при ускладненій вагітності втричі перевищував рівень нешкідливості (до 0,005 мг/л) та в 2,8 раза показник при неускладненій гестації. У 44,0 % жінок кадмій визначався в «насторожуючих» межах, а в 40,0 % виявлено потенційно шкідливий його рівень. Найбільший вміст кадмію зафіксовано при загрозі переривання вагітності, що в 3,2 рази перевищував рівень при фізіологічній гестації. Водночас у жінок з анемією вміст кадмію був у 2,4 раза вищим, ніж у здорових вагітних.

Висновки. В сучасних екологічних умовах на фоні підвищеного надходження абіотичних речовин доцільним є впровадження в практичну охорону здоров'я дослідження вмісту в крові свинцю та кадмію на ранніх термінах вагітності як чинників ризику розвитку гестаційних ускладнень, що в свою чергу забезпечить збереження здоров'я жінки та дитини.

Ключові слова: вагітність, свинець, кадмій, гестаційні ускладнення.

INTRODUCTION

Considering intensive chemical environmental pollution, health care is one of the priority problems in modern medicine [19]. Nowadays, heavy metals, particularly lead and cadmium, which are classified as global environmental pollutants, adversely affect public health. Even low concentrations of these metals and their compounds can accumulate and result in decrease of adaptive body reserves. Under such conditions, generative function is among the least protected and most susceptible ones [4, 23]. In this regard, the concept of reproductive health as a sensitive indicator of ecological problem was stated [7, 21].

Environmental pollution has an active harmful impact on children's health, because of their high sensitivity to the effects of heavy metals throughout all periods of growth and development, including the intrauterine stage [6, 8, 9, 13].

High lead toxicity and ability to accumulate in organs and tissues endanger penetration

of metals into the human body via various routes with further development of various toxic effects, including remote and irreversible ones due to the affection of the cell genome [19, 20].

Correlation between elevated levels of lead in the blood and the development of threatened abortion and premature birth syndrome has been detected [12]; *lead excess can cause miscarriage*, intrauterine growth retardation, chronic fetal hypoxia, bleeding during pregnancy and labor, and occurrence of birth defects in infants [2, 5, 8, 14, 22]. Even very low levels of lead in the fetal blood can lead to a significant reduction of a child's mental abilities [8].

In *experiments on animals*, it has been shown that *inhalation of cadmium* can cause fewer offspring and higher frequency of congenital malformations, namely embryotoxic and teratogenic effects, and in adults – liver damage and alterations in the immune system [3, 15]. A controversial issue is the impact of high levels of placental cadmium on reduction of

neonatal anthropometric data (weight, height, chest *circumference*) [10, 16].

The acceptable concentration of lead in the blood for adults is considered 0.2 mg/l. The range 0.2-0.4 mg/l is "alert" and rated as "metal carriage". The exceeding of 0.4 mg/l is regarded as a potentially harmful level [11, 20].

The US Center for Disease Control developed officially acceptable medical standards of blood lead levels for children and adults, according to which the content below 0.1 mg/l is considered a physiologically acceptable maximum. If lead level in a pregnant woman's blood is higher, the same level is likely to be in her newborn child, which can cause disorders of psychological development. In children, lead content 0.1-0.19 mg/l is estimated as increased, 0.2-0.44 mg/l – high, and 0.45-0.69 mg/l – very high level; concentration above 0.7 mg/l is considered extremely high and requires immediate treatment [2].

An acceptable level of cadmium in the blood for an average person is considered 0.007 mg/l ranging within 0.004-0.013 mg/l [18], for occupational exposure, according to American Conference of Governmental Industrial Hygienists (ACGIH), – 0.005 mg/l [1]. The suggested reference levels of cadmium in adults' blood are the following: a modified norm – up to 0.005 mg/l; the level of "alertness" – 0.005-0.01 mg/l; potentially harmful level – above 0.01 mg/l [11].

Thus, considering an increase in basic content of priority environmental pollutants, during pregnancy a woman's body is under their harmful influence. In this regard, a scientific search for risk factors of potential adverse effect on the gestation process for timely implementation of adequate preventive and corrective measures is an important issue. Thus, the aim of this study was to evaluate lead and cadmium levels in women's blood in uncomplicated and complicated pregnancy and to assess the significance of their influence on the gestational process.

MATERIALS AND METHODS

To achieve the aim, lead and cadmium levels in the blood of 92 pregnant women were investigated. The women were under medical supervision in prenatal first city community clinic in

Lviv. The selection criteria were the following: the first trimester of pregnancy, homogeneity of social status, absence of physical, *genetic* and *oncological* diseases, burdened obstetric and gynecological history. The metal content in the blood was investigated in 42 women with uncomplicated pregnancy and 50 women with gestation complicated by anemia (44.0 %) and threatened abortion (56.0 %). The course of pregnancy was analyzed by statistical processing of primary documents – individual map of pregnant and parturient women (form 111/o).

Determination of metals was evaluated by inversion voltammetry method. Preparation of blood samples was conducted in the *Central Research Laboratory and Laboratory of industrial toxicology* of Danylo Halytsky Lviv National Medical University. Measurements were carried out using voltammetry analyzer AVA-2 in the Sanitary Epidemiological Station of Lviv Railway.

Results. An average concentration of lead in the blood of women with uncomplicated gestation was 0.124 ± 0.017 mg/l, which corresponds to generally accepted levels. However, in 11.9 % of pregnant women, metal content was detected within 0.2 to 0.4 mg/l, which is rated as "carriage" [20]. Disturbing is the fact that in 4.8 % of women, lead concentrations slightly exceeded the upper level of acceptable content (> 0.4 mg/l). Thus, blood lead level corresponded to the existing norms in 83.3 % of women with physiological pregnancy, in the rest of women it exceeded the limit, that will contribute to a similar tendency to its content increase in a child's blood.

Comparing the results with the data of the Center for Disease Control [2], physiologically acceptable level of lead (0.1 mg/l) was determined in 57.1 % of women with uncomplicated gestation. Exceeding of this level was detected in 42.9 % of pregnant women, lead concentrations ranged within 0.1-0.19 mg/l in 61.1 % of them, which, according to the reviewed literature [17], causes hypertension in adults and leads to lower IQ, hearing, and growth in children. According to data [2], children may have problems with behavior and learning. In 27.8 % of women, lead concentrations in the blood constituted from 0.2 to 0.44 mg/l, which causes *neurological disorders* and intellectual decline in children. It is disturbing to determine the lead level above 0.45 mg/l in 11.1 % of

women, which, according to the US data, is too high and without timely medical aid is dangerous for children's health.

The average level of lead in complicated pregnancy was 0.295 ± 0.027 mg/l, that is defined as "alertness" and was reliably ($p < 0.05$) 2.4 times higher than in women with uncomplicated course of gestation (Table 1). "Carriage" was found in 54.0 % of women, and potentially harmful level of lead (> 0.4 mg/l) was observed in 24.0 % of blood samples. The highest concentration of metal – 0.315 ± 0.033 mg/l was recorded in the blood of women with threatened miscarriage, which was by 154.0 % higher ($p < 0.05$) than in uncomplicated pregnancy. At the same time, lead level in women with anemia exceeded the index in physiological gestation by 95.2 % ($p < 0.05$).

Table 1.

**Content of lead in the women's blood
(M ± m)**

Course of pregnancy		Lead content, mg/l
Uncomplicated pregnancy	42	0.124 ± 0.017
Complicated pregnancy	50	$0.295 \pm 0.027^*$
Threatened abortion	28	$0.315 \pm 0.033^*$
Anemia	22	$0.242 \pm 0.034^*$

Note * – $p < 0.05$ as compared with uncomplicated pregnancy

In comparison with the data of the Center for Disease Control (USA), physiologically acceptable level of lead was determined only in 12.0 % of women with complicated gestation. In 88.0 % of women (in anemia – 86.3 %, threatened abortion – 89.2 %), exceeding of the maximal physiologically acceptable level is observed. Among them, in 63.6 % cases lead concentrations ranged within 0.2-0.44 mg/l, which is regarded as being high for children and "alarming" for adults. In 25.0 % of women, lead level was above 0.45 mg/l, which, as noted above, is considered potentially dangerous for adults and without timely medical care is dangerous for children's life.

It was established that the level of cadmium in the blood of the women with physiological pregnancy was equal to 0.0054 ± 0.0008 mg/l, i.e. relevant with the known options for an average person (< 0.013 mg/l) and slightly high-

er than recommended by the American Conference of Governmental Industrial Hygienists (0.005 mg/l). If compared with the approximate reference level of cadmium in the adults' blood [16], cadmium content was determined within 0.005 – 0.01 mg/l in 33.4 % of women with uncomplicated gestation, which is estimated as the level of "alertness", and potentially harmful levels were found in 9.5 % of cases. Thus, cadmium content corresponded to the existing norms in 57.1 % of pregnant women among the total number of surveyed women with physiological pregnancy, in the rest women it exceeded this limit 1.8-2.2 times, which will promote an increase in its content in the children's blood.

The average level of cadmium during complicated pregnancy was 0.0152 ± 0.0025 mg/l, that exceeded thrice the acceptable level and 2.8 times ($p < 0.05$) the index in uncomplicated gestation (Table 2). In 44.0 % of women, cadmium was determined in "alert" range, potentially harmful level was found in 40.0 %. The highest content of cadmium – 0.0171 ± 0.0031 mg/l – was recorded in threatened miscarriage which exceeded the index in physiological gestation 3.2 times ($p < 0.05$). However, pregnant women with anemia had 2.4 times higher cadmium level ($p < 0.05$) than healthy ones.

Table 2.

**Content of cadmium in the women's blood
(M ± m)**

Course of pregnancy		Cadmium content, mg/l
Uncomplicated pregnancy	42	0.0054 ± 0.0008
Complicated pregnancy	50	$0.0152 \pm 0.0025^*$
Threatened abortion	28	$0.0171 \pm 0.0031^*$
Anemia	22	$0.0130 \pm 0.0035^*$

Note * – $p < 0.05$ as compared with uncomplicated pregnancy

Conclusions

In complicated gestation, the lead level was detected in the "alarming" range (0.2-0.4 mg/l) and was 2.4-3.1 times higher than recommended by the US researchers (0.1 mg/l), while the cadmium content exceeded acceptable level (0.005 mg/l) 3 times and 1.3-1.7 times – potentially harmful level (0.01 mg/l). The excess of acceptable levels of lead was de-

tected in 78.0 % of women with complicated pregnancy, of cadmium – in 84.0 %, whereas during the physiological gestation – in 16.7 % and 42.9 % women, respectively. Lead levels higher 1.9-2.5 times ($p < 0.05$) and concentration of cadmium higher 2.4-3.2 times ($p < 0.05$) were found in all groups of women with complicated pregnancy compared with uncomplicated pregnancies.

Thus, nowadays in ecological conditions with increased levels of abiotic substances, it is reasonable to implement detection of lead and cadmium contents into practical health care, especially in early gestation, as risk factors for development of gestational complications, which in its turn can protect the health of women and newborns.

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Стаття надійшла 11.10.2016

Після допрацювання 02.12.2016

Прийнята до друку 16.11.2016