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Influence of Pb and Cd levels in whole blood of postmenopausal women on the incidence of anxiety and depressive symptoms

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Abstract

Introduction. To-date, the influence of heavy metals such as Pb or Cd on mental functioning, and especially on the occurrence of depressive and anxiety-related disorders, has not been well understood.

Objectives. 1) Assessment of Pb and Cd levels in whole blood of postmenopausal women. 2) Assessment of the severity of anxiety and depressive symptoms depending on Pb and Cd levels in whole blood of postmenopausal women.

Materials and method. The survey-based study involved 198 healthy postmenopausal women from West Pomeranian province in Poland. It was performed using the Primary Care Evaluation of Mental Disorders (PRIME-MD), Beck's Depression Inventory (BDI), and the State-Trait Anxiety Inventory (STAI). The second part of the study was based on biochemical analysis of the levels of heavy metals (Pb, Cd).

Results. The mean level of Pb was 19.85 ± 8.99 µg/l and Cd 0.87±0.98 µg/l; these levels were within normal ranges. Analysis of the mean levels of Pb and Cd in whole blood of postmenopausal women in relation to the severity of depressive symptoms did not reveal statistically significant differences. Correlation analysis demonstrated a statistically significant ($p<0.05$) negative correlation (-0.22) between the level of Pb and the severity of anxiety as a state. Correlations between the levels of Pb and Cd and the severity of anxiety as a trait were not statistically significant.

Conclusions. The mean Pb and Cd levels in whole blood of healthy postmenopausal women did not exceed acceptable limits. The study did not confirm a relationship between the levels of selected heavy metals and the severity of anxiety and depressive symptoms in healthy women. However, there was a relationship between the level of Pb and the severity of anxiety as a state.

Key words

Pb, Cd, depressive disorder, anxiety, postmenopausal women

INTRODUCTION

There are many reports indicating a negative influence of environmental pollutants on the human body. However, to-date, the influence of heavy metals such as Pb or Cd on mental functioning, and especially on the occurrence of depressive and anxiety-related disorders has not been well understood [1]; therefore, the presented research and analysis were undertaken with the aim of assessing the dependence between concentrations of heavy metals (Pb and Cd) in the blood serum, and the severity of depression and anxiety symptoms. The research involved postmenopausal women, due to the particularly high exposure to the occurrence of this type of disorders in people forming this group. Depression is a disorder that mainly concerns females (females are affected 2–3 times more often than males) [2, 3]. In the perimenopausal period, 20–30% of women experience depressive disorders that require treatment, and in 90% it shows weaker mood disorders, i.e.: difficulty in concentrating, irritability and emotional lability as a direct result of hormonal changes [4]. It is also often related to hormonal changes that end the procreative phase, cessation of menstruation, vaginal dryness leading to a decrease in libido, dyspareunia, frequent infections in the genito-urinary tract, urinary incontinence and pelvic organ prolapse. During menopause, a significant increase in hospitalizations for depression can be observed which may be associated with a higher frequency of severe depression [5].

Anxiety is an interdisciplinary problem characterized by high complexity and multi-dimensionality. It is a negative emotion with an accompanying strong sense of danger and signs of severe psychomotor and autonomous agitation. Single panic attacks are reported by approximately 15% of the general population, whereas the distribution of anxiety disorders with panic attacks occurs in 3–3.5%, on average, and is approximately two to three times more common in women [6].

Due to the lengthening of life expectancy, as well as demographic processes that cause ageing, women's health problems associated with menopause and ovarian steroid deficiency have become an important public health issue. In

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the last century, the average age of women's lives exceeded the age of menopause, and currently approximately 30% of a woman's life coincides with the postmenopausal period [7].

Pb is a highly toxic element with a multivisceral activity. It enters the human body mainly orally through the respiratory system, and to a much lesser extent through the skin [8]. It causes damage of varying severity; from temporary changes to persistent organic ones. Shortly after entering the body it is transported to soft tissues and organs, such as the liver, kidneys, lungs, brain, spleen, muscles and heart. After a few weeks, most of the Pb accumulates in bone tissue. Approximately 94% in adults, and approximately 73% in children of the total Pb contained in the body accumulates in bones and teeth. The time span of its life in soft tissues is about 30 days, and in bones – approximately 40 – 90 years. A portion of Pb can be stored in bones for decades, and the remaining portion may leave the reservoir and return to the blood stream or move to other organs in certain specific situations such as pregnancy, lactation, bone fractures or advanced age [9]. Pb can greatly affect the formation of physiological and biochemical disorders. It has been shown that a consequence of occupational exposure to this element is damage to DNA [10].

Pb has the most damaging effect on the nervous system. If exposure to high doses occurs, Pb can severely damage the brain and kidneys, leading to death [9].

Cd is a metal toxin that adversely affects the functioning of the human body. It enters the human body orally in 80%, through the respiratory tract in 19% and by contact in 1% [8]. This element induces breaks in the chains of the deoxyribonucleic acid, DNA, and numerous chromosomal aberrations. Numerous organizations involved in public health activities, such as the Environmental Protection Agency (EPA), Department of Health and Human Services (DHHS), and International Agency for Research on Cancer (IARC), identify Cd as a carcinogenic factor to humans [11]. It has been shown that in workers exposed to inhalation of Cd lung cancers were diagnosed more frequently.

In 1999, Cd was recognized by the Agency for Toxic Substances and Disease Registry as one of seven substances found in the environment that have a particularly negative impact on human health [12]. A minimum harmful dosage of Cd which is delivered orally in the medium-long term, i.e. from 15 – 364 days, is considered to be an amount of 0.5 mg of Cd/kg/day. The lowest dose for humans which at a shorter time (14 days) would give signs of acute Cd poisoning has yet to be determined. However, long-term exposure to low doses of Cd in inhaled air can cause integration of this metal in the structure of the kidneys which can result in diseases of this organ. As a result of constant exposure to Cd there was also observed a formation of respiratory diseases with dyspnoea, cough, rales, and impaired lung functions [13]. Among the general population, consumption of food and water with a high content of Cd can cause irritation of the stomach, resulting in vomiting or diarrhoea and, in some cases, in death. The consequence of such exposure can be bone fragility, reflected in susceptibility to fractures. Research on laboratory animals have confirmed the dependence between exposure to Cd and occurrence of diseases of the kidneys and bones. It was further found that Cd causes anaemia, liver, brain and nerve damage. In relation to people, there is no clear evidence of the existence of a dependence between elevated Cd and these conditions [14].

OBJECTIVES

1. Assessment of Pb and Cd levels in whole blood of postmenopausal women.
2. Assessment of the severity of anxiety and depressive symptoms depending on Pb and Cd levels in whole blood of postmenopausal women.

MATERIALS AND METHOD

The research was conducted among 198 healthy postmenopausal women, residents of the West Pomeranian Province in Poland. Women were selected according to the following criteria: postmenopausal period confirmed by the absence of menstruation for at least a year, no use of the menopausal hormone therapy (MHT), no history of psychiatric treatment, no tumours, no thyroid diseases or diabetes, no addictions (alcohol and cigarettes), correct blood pressure parameters.

The first part of the research was carried out using the diagnostic survey method. The study used standardized research tools:

– PRIME-MD questionnaire to exclude women with axis I psychiatric disorders according to ICD-10 [15];
– Beck's Depression Inventory [16] – frame-of-mind self-examination inventory for determining depression. The following standards were used: no depression (0–11), mild depression (12–26), moderate (27–49), and severe (50–63);
– STAI Physical Inventory and Anxiety Characteristics by C. D. Spielberger, R. L. Gorsuch, R. E. Lushene, was designed to test anxiety understood as temporary and conditional on the situation status of an individual, and anxiety understood as a relatively stable personality trait. It consists of two questionnaires: X1 (anxiety as a state) and X2 (anxiety as a characteristic), each of which contains 20 questions.

The second part of the study was biochemical research of the concentration of the toxic metals Pb and Cd.

After obtaining consent to participate in the research, 5 ml of blood was taken from each patient to determine the concentration of Pb and Cd. Blood was collected from the blood vessel in a closed system (Vacutainer) into a tube with an anticoagulant. The biological material was stored at -20 °C. Blood in refrigerated conditions was transported to the Institute of Occupational Medicine and Environmental Health functioning at the Department of Chemical Harmfulness in Sosnowiec, Silesia. Determination of metal toxins was made in the Laboratory of Analysis of Metals. The analytical procedure was based on the method by Stoppler and Brandt. In the blood sample deproteinized with nitric acid the concentration of Pb and Cd in the supernatant fluid was made using atomic absorption spectrometry with electrothermal atomization of a sample (GFAAS). The non-specific absorption correction included Zeeman's background correction. The measurement was made using atomic absorption spectrometer – Perkin Elmer 4100ZL. Research conducted in this facility is subject to regular quality control through participation in the national and international system of research quality control of the Institute of Occupational Medicine in Łódź, Poland, the Istituto Superiore di Sanita in Rome, Italy, and the CDC in Atlanta, USA. The laboratory

has been certified by the German Society of Occupational Medicine and Environmental Medicine e.v., at the Friedrich-Alexander University of Erlangen-Nuremberg, Germany.

The maximum admissible concentration of Pb, as interpreted by the Laboratory, was a value of less than 100 mg/l, while the correct value of Cd in whole blood, according to the guidelines of the Institute of Occupational Medicine Environmental Health, was 1.5 mg/l.

The research was approved by the Bioethics Committee [cover for blind review] No. KB-0012/154/12.

Statistical analysis. Pearson's linear correlation coefficient and Spearman's rank correlation coefficient were used to measure the strength of an association between two variables. For the linear correlation between continuous variables which meet the assumption of linear normality. In the case of rank correlation, at least one variable had values presented on the ordinal scale. The results were interpreted using the r/R coefficient and the corresponding probability value (p).

The Student's t-test and Mann-Whitney U test wereused to verify the null hypothesis about the lack of differences concerning quantitative variables between two groups of women. The choice of test depended on confirmation of the normality of the variable distribution.

One-way analysis of variance (ANOVA) was used to verify the following null hypothesis: many groups of women (more than two) are identical in terms of arithmetic means of particular quantitative variables. This was in contradiction of the following alternative hypothesis: statistically significant differences concerning the variables analyzed are observed between at least two groups of women. The results of analysis are shown in the form of F-statistics and p-value. The null hypothesis was rejected in support of the alternative hypothesis if the p-value was below or equal to α.

Characteristics of the study group. The average age of studied women was 56.26±5.55 years; median – 55 years; the youngest studied woman was 42-years-old and the oldest was aged 70. More than half of studied women (56%) had secondary education and 32% of patients had higher education. Most women were residents of cities, of which 62% came from cities with population of over 100,000 inhabitants and 23% from smaller towns with a population of 10,000 – 100,000 inhabitants. Married women accounted for 69% of patients, those economically active women accounted for 65% of the respondents.

Methods used were descriptive statistics and correlation. Statistical calculations were based on the "Statistica PL" software. During the analysis of Pb and Cd in the context of the level of anxiety and depression in women after menopause, the following statistical methods were used:

RESULTS

Analysis of the average concentrations of Pb and Cd in whole blood depending on severity of depression showed no statistically significant differences. It was shown that the average concentration of Pb in post-menopausal women amounted to 19.85±8.99 μg/l and was within the normal range (below 100 μg/l). The highest concentration of Pb was found in women who experienced severe symptoms of depression (23.70±12.70 μg/l), and the lowest among women with average depression (15.48±5.14 μg/l). The lowest concentration of Cd (0.48±0.28 μg/l) occurred in women who had severe symptoms of depression, and the highest in women who did not show symptoms of depression (0.94±1.11 μg/l). The average concentration of this metal in all postmenopausal women was 0.87±0.98 μg/l and ranged in the widely accepted norms (1.5 μg/l) (Tab. 1).

Table 1. Average concentration of Pb and Cd in whole blood of women surveyed and severity of depression

Depression	n		Min-max	Me	Q_1–Q_3
Pb (μg/l)					
None	128	20.79±9.38	3.00–56.00	19.50	14.00–25.00
Mild	39	18.18±7.22	4.00–32.00	18.00	13.00–24.00
Average	21	15.48±5.14	7.00–27.00	15.00	13.00–17.00
Severe	10	23.70±12.70	9.00–44.00	21.50	12.00–37.00
Total	198	19.85±8.99	3.00–56.00	18.00	13.00–24.00
Cd (μg/l)					
None	128	0.94±1.11	0.15–8.65	0.55	0.39–1.03
Mild	39	0.77±0.73	0.14–3.08	0.50	0.32–0.86
Average	21	0.85±0.67	0.15–2.38	0.58	0.42–1.03
Severe	10	0.48±0.28	0.13–1.15	0.47	0.34–0.57
Total	198	0.87±0.98	0.13–8.65	0.53	0.36–0.98

N – number of surveyed women; – standard deviation; Min-Max – minimum and maximum values; Me – Median; Q_1 – lower quartile; Q_3 – higher quartile

Analysis of data resulting from the assessment of concentrations of Pb and Cd in postmenopausal women was made taking into account patients in whose self-esteem there were symptoms of depression (n=70) (mild, medium, and heavy), and in whom these symptoms were not diagnosed (n=128). No statistically significant differences (p>0.05) in average concentrations of Pb and Cd in women without symptoms of depression, compared to women who had those symptoms (Tab. 2).

Table 2. Average concentration of Pb and Cd in whole blood of postmenopausal women with no depression and characteristics of depression

Metals	No depression n=128	Depression n=70	T/Z*	p
	$\overline{X}$+SD	$\overline{X}$+SD		
Pb (μg/l)	20.79 ± 9.38	18.16 ± 8.00	1,857916[Z]	>0.05
Cd (μg/l)	0.94 ± 1.11	0.75 ± 0.67	1.322346[t]	>0.05

$\overline{X}$+SD – standard deviation; t/Z – coefficients and p-values for Student's t-test / Mann– Whitney U test; p – level of significance; T/Z – Mann-Whitney's test probability factor';
p – level of significance

The correlation between severity of depression and the concentration of Pb and Cd in postmenopausal women was not statistically significant (p>0.05) (Tab. 3).

Table 3. Analysis of correlation between severity of depression and concentration of Pb and Cd in whole blood of patients after menopause

Depression				
Metals	n	R	t (N-2)	P
Pb (μg/l)	198	-0.131930	-1.86330	>0.05
Cd (μg/l)	198	-0.081329	-1.14239	>0.05

R – Spearman's rank correlation coefficient; t(N-2) – Test statistics to check significance of R correlation coefficient; p – significance level calculated for R

Analysis of Pb concentrations in whole blood of postmenopausal women showed statistically significant differences ($p<0.01$) between the concentration of Pb in the blood of studied women and the intensity of anxiety assessed in the STAI-X1 questionnaire. The highest concentration of Pb in whole blood was obtained in women with no anxiety (22.84±9.79) while the lowest (17.20±7.52) in women who experienced anxiety defined as a condition. There was no such dependence with respect to the concentrations of Cd in whole blood of women surveyed after menopause. The highest concentration of Cd was also demonstrated in women with no anxiety (0.98±0.80), and the lowest (0.73±0.71) in women with anxiety assessed as a condition, but the differences were not statistically significant. Data analysis showed that the highest concentration of Pb in whole blood (21.06±9.56) was found in women with no evidence of anxiety as a characteristic, and the values were higher than those obtained in the whole group of female patients (19.86±8.99). The lowest concentration of this metal (19.14±8.70) was observed in women who experienced anxiety as a characteristic, and this value was similar to the case of women with the anxiety standard (19.61±8.86) ($p>0.05$). For the concentration of Cd, the highest average level was observed in women with the anxiety standard as a characteristic (0.93±1.20), and the lowest (0.79±0.67) with the anxiety characteristic ($p<0.05$) (Tab. 4).

Table 4. Average concentration of Pb and Cd in blood and severity of anxiety as a STAI-X1 condition and a STAI-X2 characteristic in postmenopausal women

	n		Min-max	Me	Q_1–Q_3	F	p
STAI-X1							
Pb (µg/l)							
No anxiety	45	22.84±9.79	5.00–56.00	22.00	16.00–27.00		
Standard	100	19.92±8.98	3.00–56.00	18.00	14.00–24.00	4.9848	<0.01
Anxiety	53	17.20±7.52	5.00–40.00	15.00	12.00–22.00		
Total	198	19.85±8.99	3.00–56.00	18.00	13.00–24.00		
Cd (µg/l)							
No anxiety	45	0.98±0.80	0.15–3.29	0.69	0.40–1.41		
Standard	100	0.90±1.16	0.15–8.65	0.52	0.37–0.95	0.8645	>0.05
Anxiety	53	0.73±0.71	0.13–3.69	0.50	0.34–0.83		
Total	198	0.88±0.98	0.13–8.65	0.53	0.36–0.98		
STAI-X2							
Pb(µg/l)							
No anxiety	50	21.06±9.56	5.00–56.00	20.50	14.00–25.00		
Standard	99	19.61±8.86	3.00–56.00	18.00	13.00–24.00	0.6388	>0.05
Anxiety	49	19.14±8.70	7.00–44.00	17.00	13.00–24.00		
Total	198	19.86±8.99	3.00–56.00	18.00	13.00–24.00		
Cd (µg/l)							
No anxiety	50	0.85±0.75	0.15–3.29	0.55	0.40–0.96		
Standard	99	0.93±1.20	0.14–8.65	0.51	0.33–0.98	0.3466	>0.05
Anxiety	49	0.79±0.67	0.13–3.03	0.52	0.40–1.03		
Total	198	0.87±0.98	0.13–8.65	0.53	0.36–0.99		

N – numberofsurveyed women; – standard deviation; Min-Max – minimum and maximum values; Me – median; Q_1 – lower quartile; Q_3 – higher quartile; F – ANOVA test

Correlation analysis showed a statistically significant ($p<0.05$) weak negative correlation (-0.22) between the concentration of Pb and intensity of anxiety as a state. The correlation between concentration of Pb and Cd and intensity of anxiety was not statistically significant (Tab. 5).

Table 5. Correlation analysis between concentration of Pb and Cd in blood and intensity of anxiety as a STAI-X1 state and anxiety as a STAI-X2 characteristic

METALS	r	p
STAI- X1		
Pb (µg/l)	-0.22	**<0.05**
Cd (µg/l)	-0.04	>0.05
STAI -X2		
Pb (µg/l)	-0.0952	>0.05
Cd (µg/l)	-0.0708	>0.05

r – Pearson's linear correlation coefficient; p – significance level calculated for r

DISCUSSION

The negative and differential influence of heavy metals on biological functions of the human body has been proven in many studies conducted by scientists worldwide, although the effects that these chemicals may have on the human mental condition are not deeply understood. In the original research, the authors analysed the impact of Pb and Cd concentrations in blood on the severity of depression and anxiety among women in the menopausal age. In the group covered by the analysis there was no dependence between the concentrations of Pb in blood and the level of depression.

Analyses carried out by other authors have pointed to the possibility of a dependence between the concentrations of these heavy metals and risk of developing depressive symptoms. In a study conducted on a group of 5,560 Americans aged 20–80 years, based on data from the US National Health and Nutrition Examination Survey, a dependence between the content of heavy metals in tested urine and the presence of symptoms of depression was observed. The study also showed the influence of other factors from environmental contaminants the greater concentration of which in urine fostered the development of depressive disorders. The findings of this study led to the conclusion that efforts should be made to eliminate harmful chemicals from the human environment, and taken into account in policy planning to ensure the mental health of the population [1]. Similarly, many studies conducted among patients diagnosed with depression and panic attacks showed an excess of Pb and/or Cd [17, 18]. In a study by Eum et al. [19], an analysis of the concentrations of bone Pb among nurses (mean age 59 years) and its connection with the occurrence of depression and anxiety disorders was made, and it was shown that the increased concentrations of Pb in the tibia in premenopausal women and those after menopause, but using MHT, was associated with a greater severity of depression and anxiety. Simultaneously, those patients showed low concentrations of Pb in blood. A study conducted on a representative group of 2,892 people aged 20–39 showed that there was a dependence between the concentration of Cd in blood and prevalence of depressive symptoms. This relation was not related to smoking. The authors concluded that their findings suggest

that limiting the exposure to Cd may affect the reduction in frequency of appearance of depression [20].

Analysis of concentrations of Cd and Pb among 61 adult patients in a psychiatric ward was made at the University Teaching Hospital, comparing their results with a control group. It was shown that the concentrations of Cd and Pb were significantly higher among patients diagnosed with depression, including schizophrenic patients, who showed higher Pb concentrations than subjects in the control group. However, a significantly lower concentration of Cd was found in patients with maniacal disorders [21]. On the other hand, Bouchard et al. investigated a total of 1,987 subjects aged 20–39 who showed higher concentrations of Pb that were associated with a greater severity of depression and panic disorders [22].

In the original research, analysis of correlation between the intensity of anxiety measured using the STAI-X1 and STAI-X2 surveys, and the concentration of selected microelements in blood of studied postmenopausal women did not show significant differences. However, a significant negative correlation between the concentration of Pb in blood and the intensity of anxiety assessed by the STAI-X1 survey as a state was observed.

It is difficult to comment on the results obtained because the literature shows that the problem of anxiety disorders primarily affects women, increases with age, and it is difficult to decide whether the main reason for disturbances concerns the hormonal changes characteristic of the postmenopausal period, or rather by individual psychosocial and environmental conditions, including the concentration of heavy metals [23]. It is believed that the pre-menopausal period is conducive to intensification of already existing mental imbalances, including anxiety disorders [24]. It should also be taken into account that the surveyed women were healthy, with no mental illnesses, and on the basis of self-assessment one could determine the severity of symptoms of depression and anxiety. Other factors could probably also have affected the level of Pb among the respondents.

CONCLUSIONS

1. The average concentration of Pb and Cd in whole blood of healthy postmenopausal women should not exceed the value adopted as acceptable.
2. Among healthy women, no dependence between concentrations of selected heavy metals and severity of depression and anxiety was observed.
3. The existence was observed of dependence between concentrations of Pb and intensity of anxiety as a state.

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REFERENCES

1. Shiue I. Urinary heavy metals, phthalates and polyaromatic hydrocarbons independent of health events are associated with adult depression: USA NHANES, 2011–2012. Environ Sci Pollut Res 2015; 22: 17095–17103.
2. Bielawska-Batorowicz E. Koncepcje menopauzy. Część I – ujęcie demograficzne i kulturowe. Menopause Review 2005; 2: 10–18.
3. Bielawska-Batorowicz E. Psychologiczne aspekty prokreacji. Katowice, Wyd. Śląsk, 2006.
4. Pertyński T. Diagnostyka i terapia wieku menopauzalnego. Wrocław, Urban & Partner, 2004.
5. Pużyński S. Depresje i zaburzenia afektywne. Warszawa, Wyd. Lek. PZWL, 2009.
6. Bruce SE, Yonkers KA, Otto MW, et al. Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: a 12-year prospective study. Am J Psychiatry 2005; 162: 1179–1187.
7. Speroff L, Fritz MA. Menopauza i okołomenopauzalny okres przejściowy. In: Jakimiuk A, editor. Kliniczna endokrynologia ginekologiczna i niepłodność, Warszawa; 2007. p. 741–745.
8. Chmielnicka J. Toksyczność metali i półmetali. In: Seńczuk W, editor. Toksykologia współczesna, Warszawa; 2006. p. 301–53.
9. Toxicological profile for lead. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry, 2007.
10. Papanikolaou NC, Hatzidaki EG, Belivanis S, et al. Lead toxicity update. A brief review. Med Sci Monit. 2005; 11(10): RA329–36.
11. Draft Toxicological profile for cadmium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry, 2008.
12. Maes M, De Vos N, Demeds P, Wauters A, Neels H. Lower serum zinc in major depression in relation to changes in serum acute phase proteins. J Affect Disord. 1999; 56(2–3): 189–194.
13. Chan OY, Poh SC, Lee HS, et al. Respiratory function in cadmium battery workers: A follow up study. Ann Acad of Med Singapore 1988; 17(2): 283–287.
14. Malacara JM, Perez-Luque EL, Martinez- Garza S, Sànchez – Marin FJ. The relationship of estrogen receptor- alpha polymorphism with symptoms and other characteristicks in post – menopausal women. Maturitas 2004; 49(2): 163–169.
15. Spitzer R, Kroenke K, Wiliams JB. Validation and utility of a self-report version of PRIME-MD: The PHQ primary care study. Primary care evaluation of mental disorders. JAMA 1999; 282(18): 1737–1744.
16. Beck AT, Ward C, Mendelson M, et al. An inventory for measuring depression. Arch Gen Psychiatry 1961; 4: 561–571.
17. Siwek M, Dudek D, Zięba A, Nowak G. Stężenie cynku w surowicy jako obwodowy marker zaburzeń depresyjnych. Farmakoterapia w Psychiatrii i Neurologii 2006; 3–4: 141–149.
18. Schlegel-Zawadzka M, Zięba A, Dudek D. Zwyczaje żywieniowe a zawartość cynku we krwi u pacjentów w chorobach afektywnych. Badanie wstępne. Żywienie człowieka i metabolizm 2000; 27: 216–219.
19. Eum KD, Korrick SA, Weuve J, Okereke O, Kubzansky LD, et al. Relation of cumulative low-level lead exposure to depressive and phobic anxiety symptom scores in middle-age and elderly women. Environ Health Perspect. 2012; 120(6): 817–23.
20. Scinicariello F, Buser MC. Blood cadmium and depressive symptoms in young adults (aged 20–39 years). Psychol Med. 2014; 45(4): 807–15.
21. Stanley PC, Wakwe VC. Toxic trace metals in the mentally ill patients. Niger Postgrad Med J. 2002; 9(4): 199–204.
22. Bouchard M, Bellinger DC, Weisskopf MG. Blood lead levels and major depressive disorder, panic disorder, and generalized anxiety disorder in U.S. young adults. Arch Gen Psychiatry 2009; 66(12): 1313–9.
23. Collins A, Landgren BM. Experience of symptoms during transition to menopause: a population based longitudinal study. In: Berg G, Hammar M, editors. The Modern Management of the Menopause, London; 1994.
24. Rickles K, Schweizer E. The clinical course and long – term management of generalizedanxiety disorder. J Clin Psychopharmacol. 1990; 10(3): 101S-110S.