

# Assessment of vitamin D level in women with abnormal uterine bleeding and chronic psychogenic stress

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*The objective:* to study the level of vitamin D (25-hydroxycalciferol – (25(OH)D) in blood serum of women with abnormal uterine bleeding (AUB) and chronic psychogenic stress.

*Materials and methods.* We examined 100 women of reproductive age with AUB and chronic psychogenic stress (basic group) and 50 patients with AUB without psychogenic chronic stress (comparison group). 30 women without AUB and chronic stress were included in the control group. AUB was diagnosis according to the Order No. 353 of the Ministry of Health of Ukraine dated April 13, 2016. The concentration of vitamin D was determined in blood serum in all the women using the ELISA method.

*Results.* The concentration of vitamin D in the blood serum in patients with AUB and chronic psychogenic stress was on 28.01 % lower compared to the controls ( $p < 0.001$ ), in the patients with AUB without psychogenic chronic stress – 13.94 % ( $p = 0.045$ ). The number of individuals with optimal concentration of vitamin D in the control group (36.67 %) was in 2.29 times higher compared to the basic group (16.00 %;  $p=0.03$ ) and in 1.41 times more compared to the comparison group (26.00 %). Suboptimal level of vitamin D had 53.33 % women in the control group, 43.00 % – basic and 58.00 % – comparison one. The rate of persons with deficiency of vitamin D among the patients with AUB and chronic psychogenic stress was in 4.56 times higher compared to the healthy women (41.00 % and 9.00 % individuals, respectively;  $p = 0.003$ ), and in patients with AUB without chronic stress – 1.78 time (16.00 % women).

*Conclusions.* There is the insufficient vitamin D concentration in women with abnormal uterine bleeding which is more severe in the persons with chronic psychogenic stress.

*Keywords:* abnormal uterine bleeding, reproductive age, chronic psychogenic stress, vitamin D.

## Оцінка рівня вітаміну D у жінок з аномальними матковими кровотечами та хронічним психоемоційним стресом

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*Мета дослідження:* вивчення рівня вітаміну D (25-гідроксикальциферолу – 25(OH)D) у сироватці крові жінок з аномальними матковими кровотечами (АМК) та хронічним психоемоційним стресом.

*Матеріали та методи.* Обстежено 100 жінок репродуктивного віку з АМК та хронічним психоемоційним стресом (основна група) та 50 хворих з АМК без хронічного психоемоційного стресу (група порівняння). До контрольної групи включено 30 жінок без АМК та хронічного стресу. Діагноз АМК встановлено на підставі Наказу МОЗ України № 353 від 13.04.2016 р. Концентрацію вітаміну D у сироватці крові визначали у всіх жінок методом імуноферментного аналізу.

*Результати.* Концентрація вітаміну D у сироватці крові у хворих з АМК та хронічним психоемоційним стресом була на 28,01 % нижчою порівняно з контролем ( $p < 0,001$ ), у пацієток з АМК без хронічного психоемоційного стресу – на 13,94 % ( $p = 0,045$ ). Кількість осіб з оптимальною концентрацією вітаміну D у контрольній групі (36,67 %) була у 2,29 раза більшою порівняно з основною групою (16,00 %;  $p = 0,03$ ) та в 1,41 раза – порівняно з групою порівняння (26,00 %). Субоптимальний рівень вітаміну D встановлено у 53,33 % жінок контрольної групи, у 43,00 % – основної та у 58,00 % – групи порівняння. Частка осіб з дефіцитом вітаміну D серед хворих з АМК та хронічним психоемоційним стресом була у 4,56 раза більшою порівняно зі здоровими жінками (41,00 % та 9,00 % осіб відповідно;  $p = 0,003$ ), а серед хворих з АМК без хронічного стресу – в 1,78 раза (16,00 % жінок).

*Висновки.* Відзначається недостатня концентрація вітаміну D у жінок з аномальними матковими кровотечами, що більш виражено в осіб із хронічним психоемоційним стресом.

*Ключові слова:* аномальна маткова кровотеча, репродуктивний вік, хронічний психоемоційний стрес, вітамін D.

## Оценка уровня витамина D у женщин с аномальными маточными кровотечениями и хроническим психеэмоциональным стрессом

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*Цель исследования:* изучение уровня витамина D (25-гидроксикальциферола – 25(OH)D) в сыворотке крови женщин с аномальными маточными кровотечениями (АМК) и хроническим психеэмоциональным стрессом.

*Материалы и методы.* Обследовано 100 женщин репродуктивного возраста с АМК и хроническим психеэмоциональным стрессом (основная группа) и 50 больных с АМК без хронического психеэмоционального стресса (группа

сравнения). В контрольную группу включено 30 женщин без АМК и хронического стресса. Диагноз АМК установлен на основании Приказа МЗ Украины № 353 от 13.04.2016 г. Концентрацию витамина D в сыворотке крови определяли у всех женщин методом иммуноферментного анализа.

**Результаты.** Концентрация витамина D в сыворотке крови у больных с АМК и хроническим психоэмоциональным стрессом была на 28,01 % ниже по сравнению с контролем ( $p < 0,001$ ), у пациенток с АМК без хронического психоэмоционального стресса – на 13,94 % ( $p = 0,045$ ). Количество лиц с оптимальной концентрацией витамина D в контрольной группе (36,67 %) было в 2,29 раза больше по сравнению с основной группой (16,00 %;  $p = 0,03$ ) и в 1,41 раза – по сравнению с группой сравнения (26,00 %).

Субоптимальный уровень витамина D установлен у 53,33 % женщин контрольной группы, у 43,00 % – основной и у 58,00 % – группы сравнения. Доля лиц с дефицитом витамина D среди больных с АМК и хроническим психоэмоциональным стрессом была в 4,56 раза больше по сравнению со здоровыми женщинами (41,00 % и 9,00 % обследованных соответственно;  $p = 0,003$ ), а среди больных с АМК без хронического стресса – в 1,78 раза (16,00 % женщин).

**Выводы.** Отмечается недостаточная концентрация витамина D у женщин с аномальными маточными кровотечениями, что более выражено у лиц с хроническим психоэмоциональным стрессом.

**Ключевые слова:** аномальное маточное кровотечение, репродуктивный возраст, хронический психоэмоциональный стресс, витамин D.

Abnormal uterine bleeding (AUB) occurs in 30 % women in reproductive age [1]. Etiological factors are divided into structural (PALM: P – polyps, A – adenomyosis, L – leiomyoma, M – malignant tumors and endometrial hyperplasia) and non-structural (COEIN: C – coagulopathy, O – ovulation disorders, E – endometrial pathology, I – iatrogenic factors and N – unclassified causes) [2]. Currently, the course and severity of the pathology is often influenced by external factors, among which a special role is given to stress. There are stress-dependent disorders of the menstrual cycle [3], which include luteal phase insufficiency [4], infertility [5], menstrual disorders [6].

However, in recent years, a special attention is paid to the study vitamin D in the development of different pathologies. It is known that vitamin D<sub>3</sub> is produced under the influence of ultraviolet radiation or enters the human body with food. Vitamin D deficiency often contributes to diseases in childhood [7], stress and mental disorders [8], autoimmune diseases, cancer, bone pathology [9] and others. Disorders of the reproductive system can also occur due to the deficiency of this vitamin, in particular, complications of pregnancy [10], menstrual disorders in adolescence [11], infertility and polycystic ovary syndrome [12], uterine leiomyoma [13, 14].

**The objective:** to study the level of vitamin D (25-hydroxycalciferol (25(OH)D)) in blood serum of women with AUB and chronic psychogenic stress.

## MATERIALS AND METHODS

100 women of reproductive age with AUB and chronic psychogenic stress formed the basic group. The comparison group consisted of 50 patients with AUB without chronic psychogenic stress. 30 healthy women with normal parameters of the menstrual cycle and without AUB and chronic psychogenic stress were included in the control group. Inclusion criteria: AUB, age 18–45 years, satisfactory condition of the sample of the material from the uterine cavity for histological examination, chronic psychogenic stress, patient consent. Exclusion criteria: pregnancy, premenstrual dysphoric disorder, acute pelvic inflammatory disease, mental disorders, blood diseases associated with coagulation disorders, hypothyroidism, hyperthyroidism, hormonal adrenal tumors, chronic intestinal diseases, severe somatic pathology.

AUB was diagnosed according to the recommendations of Order N 353 of the Ministry of Health of Ukraine «On approval and implementation of medical and technological documents for standardization of medical care for abnormal uterine bleeding» dating 13.04.2016 and the Unified Clinical Protocol of primary, secondary (specialized) and tertiary (highly specialized) medical care for abnormal uterine bleeding [2]. The presence of chronic psychogenic stress was exposed on the basis of a clinical interview with a psychologist. The level of stress was assessed by the Perceived Stress Scale-10, PPS-10 [15]. The higher the indicators demonstrate the higher the stress level. The research was performed in «Kreminna Multidisciplinary Hospital of Kreminna District Council» and approved by the Ethics Commission of the Shupyk National Medical Academy of Postgraduate Education (protocol N1 dating 15.01.2018).

The concentration of vitamin D (25-hydroxycalciferol (25(OH)D)) was determined in the blood serum by ELISA method using a set of reagents DBS-Diagnostics Biochem Canada Inc. Optimal level of vitamin D was in the ranges of 30-50 ng/ml, suboptimal level – 21–29 ng/ml, vitamin D deficiency – less than 20 ng/ml [16]. The program Statistica10 was used to process the results. The criterion  $\chi^2$  and Mann-Whitney test were used to compare the data of the the groups.

## RESULTS AND THEIR DISCUSSION

The average age of women with AUB was similar in both groups, 31.09±0.60 years in the basic group and 33.06±0.91 – in the comparison one. However, in the control group this indicator was significantly lower (26.33±0.87 years;  $p < 0.001$ ) than in women with AUB. The average mean of body mass index was 22.37±0.35 kg/m<sup>2</sup> in the basic group, 23.89±0.43 kg/m<sup>2</sup> – in the comparison group and 23.69±0.47 kg/m<sup>2</sup> – in control one. The level of perceived stress in patients with AUB and chronic stress (32.24±0.44) was increased in 1.97 times relative to healthy women (16.33±0.64;  $p < 0.001$ ), and in patients with AUB without chronic stress – 1.12 times (18.24±0.66).

The clinical parameters of the menstrual cycle were: normal frequency of menstruations had 73 (73.00 %) patients in the basic group and 41 (82.00 %) – comparison one, frequent menstruations – 23 (23.00 %)

and 8 (16.00 %) persons, respectively, infrequent menstruations – 4 (4.00 %) and 1 (2.00 %); normal duration of the menstrual bleeding – 66 (66.00 %) and 34 (68.00 %), prolonged menstrual bleeding – 34 (34.00 %) and 16 (32.00 %); regular menstrual cycle – 64 (64.00 %) and 36 (72.00 %), irregular – 36 (36.00 %) and 14 (28.00 %); normal volume of the monthly blood loss – 68 (68.00 %) and 32 (64.00 %), heavy menstrual bleeding – 27 (27.00 %) and 18 (36.00 %), light menstrual bleeding had 5 (10.00 %) patients in the basic group; 45 (45.00%) women in the basic group and 19 (38.00 %) persons in the comparison group had intermenstrual bleeding; 8 (8.00 %) and 1 (2.00 %) patients, respectively – unscheduled bleeding on progestin, estrogen gonadal steroids.

The causes of the AUB according to the PALM-COEIN classification in the patients with AUB: polyps were diagnosed in 8 (8.00 %) patients in the basic group and 10 (20.00 %) – comparison one, adenomyosis – 15 (15.00 %) and 8 (16.00 %) persons, respectively, leiomyoma – 24 (24.00 %) and 18 (36.00 %), hyperplasia of endometrium – 9 (9.00 %) and 5 (0.00 %), ovulation dysfunction – 36 (36.00 %) and 5 (10.00 %), endometrial factor – 8 (8.00 %) and 4 (8.00 %). In the basic group the number of ovulatory disorders was in 3.36 times more than in the comparison group ( $\chi^2 = 10.07$ ;  $p = 0.001$ ), leiomyoma – in 1.50 times less. Besides this, premenstrual syndrome was found in 57 (57.00 %) women with AUB and chronic psychogenic stress, 13 (26.00 %) – with AUB without chronic psychogenic stress and 5 (16.67 %) healthy individuals, algo-/dysmenorrhea – 41 (41.00 %), 11 (22.00 %) and 3 (10.00 %), respectively, chronic salpingitis and oophoritis – 24 (24.00 %), 10 (20.00 %) and 5 (16.67 %), polycystic ovary syndrome – 3 (3.00 %) and 1 (2.00 %) persons in groups with AUB.

The concentration of vitamin D in the blood serum was significantly lower in patients with AUB than in healthy women. Thus, in women in the basic group its level was on 28.01 % lower compared to controls ( $21.49 \pm 0.76$  ng/ml and  $29.85 \pm 1.68$  ng/ml; respectively;  $p < 0.001$ ), in patients in the comparison group – on 13.94 % ( $25.69 \pm 1.04$  ng/ml;  $p = 0.045$ ). Optimal concentration of vitamin D was in 11 (36.67 %) control persons, that was in 2.29 times higher than in the basic group (16 (16.00 %) patients,  $\chi^2 = 4.80$ ,  $p = 0.03$ ) and in 1.41 times more compared to the comparison group (13 (26.00 %) individuals). Suboptimal level of vitamin D had 16 (53.33 %) women in the control group, 43 (43.00 %) – basic and 29 (58.00 %) – comparison one. The rate of deficiency of vitamin D in patients with AUB and chronic stress was increased in 4.56 times compared to the healthy women (41 (41.00 %) and 3 (9.00 %) individuals, respectively;  $\chi^2 = 8.57$ ;  $p = 0.003$ ), and in patients with AUB without chronic stress – 1.78 time (8 (16.00 %) women).

Vitamin D deficiency was found in the patients with different reproductive pathologies. In patients with chronic AUB and posthemorrhagic anemia caused by adenomyosis and polyps the concentration of vitamin D was decreases till  $49.6 - 49.7 \pm 26.2$  nmol/l [17]. It's known that hypovitaminosis of vitamin D is a risk factor for the development of uterine fibroids [18]. That is why additional use of vitamin D during the treatment of uterine fibroids is an effective approach of the management to correct the uterine sizes, severity of the symptoms and improve the quality of life of the patients. The results of our study correspond with these researches.

## CONCLUSIONS

There is the insufficient vitamin D concentration in women with abnormal uterine bleeding which is more severe in the persons with chronic psychogenic stress.

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## REFERENCES

- Munro MG, Critchley HOD, Fraser IS, FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet.* 2018;143(3):393-408. doi: 10.1002/ijgo.12666.
- Ministerstva okhorony zdorovia Ukrainy. Pro zatverdzhennia ta vprovadzhenia medyko-tekhnologichnykh dokumentiv zi standartyzatsii medychnoi dopomohy pry anomalnykh matkovykh krovotekakh [Internet]. 2016. Nakaz № 353. 2016 Apr 13. Available from: <https://zakon.rada.gov.ua/rada/show/v0353282-16#Text>.
- Kuznetsova IV, Burchakova MN, Burchakov DI, Khadzhieva NK, Filippova GG. Psychogenic stress-dependent disorders of menstrual cycle: role of non-hormonal correction. *Health Woman.* 2018;10(136):68-72.
- Tatarchuk TF, Cossey NV, Tutchenko TN. Treatment of stress-induced luteal phase deficiency. *Health Woman.* 2016;3(109):18-23.
- Kosei NV, Reheda SI, Iarotska NV, Gorokhova GO. Stress infertility. *Reprod Endocrinol.* 2016;5(31):12-21.
- Grishchenko OV, Bobrytska W. New patterns of menstrual disorders' treatment – unification of the method. *Reprod Endocrinol.* 2019;3(47):26-32.
- Pavlyshyn HA, Shulhai A-MA. Vitamin D status in the pathogenesis of child diseases development. *Acta Probl Ped, Obst Gynecol.* 2018;(1):25-31.
- Chen L, Zhu H, Harshfield GA, Treiber FA, Pollock JS, Pollock D, et al. Serum 25-Hydroxyvitamin D Concentrations Are Associated with Mental Health and Psychosocial Stress in Young Adults. *Nutr.* 2020;12(7):1938. doi: 10.3390/nu12071938.
- Lips P. Vitamin D physiology. *Prog Biophys Mol Biol.* 2006;92(1):4-8. doi: 10.1016/j.pbiomolbio.2006.02.016.
- Manasova GS, Andrievsky AG, Didenkul NV, Shpak IV, Turchyn MI, Kuzmin NV. Role of the hormonal system "vitamin D/vitamin D receptors" in the formation of some pregnancy complications. *Reproductive Endocrinology.* 2020;1(51):65-8. doi: 10.18370/2309-4117.2020.51.65-68.
- Dynnik VO, Dynnik OO, Druzhynina AY. Vitamin d level and hormonal status association in adolescent girls with oligomenorrhea. *Reprod Endocrinol.* 2021;6(62):59-62.
- Khmil MS, Khmil SV, Chudiovych Nya, Khmil-doswald AS, Malanchuk LM.

- Efficiency of vitamin d using in complex treatment of infertility in women with polycystic ovary syndrome. Act Probl Peditr, Obstetr Gynecol. 2019;(2):103-10.
13. Porcaro G, Santamaria A, Giordano D, Angelozzi P. Vitamin D plus epigallocatechin gallate: a novel promising approach for uterine myomas. Eur Rev Med Pharmacol Sci. 2020;24(6):3344-3351. doi: 10.26355/eurrev\_202003\_20702.
14. Ciebiera M, Włodarczyk M, Ciebiera M, Zaręba K, Łukaszuk K, Jakiel G. Vitamin D and Uterine Fibroids-Review of the Literature and Novel Concepts. Int J Mol Sci. 2018;19(7):2051. doi: 10.3390/ijms19072051.
15. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24(4):385-96.
16. Pludowski P, Karczmarewicz E, Bayer M, Carter G, Chlebna-Sokol D, Czech-Kowalska J, et al. Practical guidelines for the supplementation of vitamin D and the treatment of deficits in Central Europe – recommended vitamin D intakes in the general population and groups at risk of vitamin D deficiency. Endokrynol Pol. 2013;64(4):319-27.
17. Pedachenko NY, Tutchenko TM, Tuchtaryan RA. Chronic abnormal uterine bleedings and quality of women's life. How to significantly improve the result? Reprod Endocrinol. 2020;1(51):14-22.
18. Ali M, Shahin SM, Sabri NA, Al-Hendy A, Yang Q. Hypovitaminosis D exacerbates the DNA damage load in human uterine fibroids, which is ameliorated by vitamin D3 treatment. Acta Pharmacol Sin. 2019;40(7):957-70. doi: 10.1038/s41401-018-0184-6.

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