ORIGINAL ARTICLE

Hormonal and vitamin D metabolic profiles in reproductive-age women with abnormal uterine bleeding and associated extragenital conditions

Liudmyla A. Vygivska, Roman Ye. Blahoveshchenskyi, Yevhen V. Blahoveshchenskyi, Yevheniya B. Radzischevska, Igor Yu. Rakytianskyi
KHARKIV NATIONAL MEDICAL UNIVERSITY, KHARKIV, UKRAINE

ABSTRACT

Aim: To assess hormonal status and vitamin D metabolic features in women of reproductive age presenting with abnormal uterine bleeding and associated extragenital conditions.

Materials and Methods: The study was conducted at the clinical base of the Department of Obstetrics, Gynecology, Pediatric Gynecology, and Medical Genetics of Kharkiv National Medical University (KhNMU). A total of 110 women of reproductive age were examined and divided into two clinical groups. The first group (main group, MG) included 80 patients diagnosed with abnormal uterine bleeding (AUB) in combination with extragenital cconditions. The second group (control group, CG) consisted of 30 somatically healthy women who presented for routine preventive examinations. Hormonal status was assessed by measuring serum concentrations of luteinizing hormone (LH), follicle-stimulating hormone (FSH), progesterone (PRG), estradiol (E2), and vitamin D using enzyme-linked immunosorbent assay (ELISA) methods. Statistical analysis was performed using the general-purpose software package Statistica 6.0.

Results: The average age of the participants was 31.5 ± 13.5 years. Among women in the main group, the most frequently observed extragenital conditions were diseases of the endocrine, circulatory, and digestive systems. Analysis of serum hormone levels revealed a decrease in FSH (1.84-fold), LH (1.64-fold), and PRG (2.6-fold) (KWT, $p < 0.01$). Conversely, E2 levels were elevated by 3.52-fold in the MG (KWT, $p < 0.01$). Serum vitamin D levels in the MG were reduced by 2.25-fold compared to the CG (KWT, $p < 0.01$). A statistically significant ($p < 0.05$) positive correlation was found between serum E2 and vitamin D levels ($r = 0.61$).

Conclusions: The study revealed distinct features of the hormonal profile and vitamin D metabolism in women of reproductive age with abnormal uterine bleeding and concomitant extragenital conditions. Specifically, this patient population demonstrated decreased serum levels of LH, FSH, PRG, and vitamin D, accompanied by hyperestrogenemia. A statistically significant correlation was observed between serum E2 and vitamin D levels.

KEY WORDS: Abnormal uterine bleeding, reproductive age, extragenital conditions, hormonal profile, vitamin D metabolism

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INTRODUCTION

Bleeding in obstetrics and gynecology is one of the most pressing problems faced by doctors worldwide [1]. Abnormal uterine bleeding (AUB) is the most common type of bleeding in gynecology [2, 3].

AUB affects up to one third of women of reproductive age and is the most debilitating symptom [4]. According to Sun Y et al., 2018 [5], this disorder of the reproductive age is the fourth most common reason for seeking gynecological services [6]. While AUB rarely poses a direct threat to life, it often leads to a substantial decline in quality of life [4].

Among the many causes of AUB, extragenital conditions (ECs) play a certain role. This is due to the characteristics of the endometrium, which depend on changes in the general hormonal background of patients. And the functional state of some organs and systems has a certain influence on the characteristics of the hormonal background [7, 8]. Thus, AUB can be caused by thyroid dysfunction, uncontrolled diabetes, metabolic disorders, changes in blood clotting (most often von Willebrand disease), various infectious diseases (influenza, pneumonia, Lyme disease, etc.), taking medications (corticosteroids, antipsychotics or antiepileptic drugs), climate change, eating habits, psychotraumatic situations, etc. [9,10]. Given the various functions of vitamin D in the body, increasing attention is paid to its use in medical practice [11,12].

Vitamin D_3 has been shown to be produced under the influence of ultraviolet radiation or obtained through dietary intake. Deficiency of this vitamin is a cause of various diseases in people of all ages. In recent years, scientists have reconsidered vitamin D as a hormone with numerous biological properties

and health benefits for patients. Historically, vitamin D was believed to primarily maintain skeletal health and regulate calcium and phosphorus balance in the body. However, recent scientific studies show a much broader spectrum of action for this vitamin [13]. It is essential for extrarenal tissues, prenatal health, brain function, immunity, pregnancy, cancer prevention, and cardiovascular health [14]. Recently, in addition to its crucial role in bone health and immune function, vitamin D has attracted increased attention for its possible influence on many processes related to women's reproductive health. Studies by Dragomir R. et al. (2024) demonstrate the role of vitamin D in maintaining adequate hormonal status, fertility, and pregnancy outcomes [15].

Research into the role of vitamin D deficiency in the development of menstrual disorders in women has recently gained wide interest. Studies have shown that taking high doses of vitamin D can lead to the restoration of the menstrual cycle (MC). Vitamin D receptors are expressed in the ovaries, placenta, and uterus. In animal experiments, dietary vitamin D deficiency reduced fertility by 45–70%, and the inability to convert vitamin D to its active form disrupted the menstrual cycle, affecting follicular development and causing anovulatory cycles. Vitamin D deficiency is a risk factor for polycystic ovary syndrome (PCOS). In women with PCOS, vitamin D supplementation can normalize the menstrual cycle and improve ovarian folliculogenesis [16, 17]. However, there are still few studies on the effects of vitamin D on menstrual function in women with AUB.

Wu Z et al. (2018) conducted a study concluding that menstrual pain is associated with low serum vitamin D concentrations [18]. Similarly, Rahnemaei FA et al. (2021) found that weekly high-dose vitamin D supplementation can reduce menstrual pain [19].

Amzajerdi A et al. (2023) demonstrated that high-dose vitamin D not only decreases pain intensity but also reduces the need for nonsteroidal anti-inflammatory drugs in women with primary dysmenorrhea and vitamin D deficiency. Consequently, they recommended including vitamin D in the treatment regimen. The authors also emphasized the need for additional clinical trials to further confirm the effectiveness of vitamin D in reducing menstrual blood loss [20].

Therefore, according to Fedosiuk KV (2022) [21], the adjunctive use of vitamin D represents a rational approach in gynecological practice and contributes to improving women's quality of life. Despite recommendations for its widespread use, it is crucial to be aware of the potential side effects of vitamin D and to administer it under close medical supervision [22].

AIM

To assess hormonal status and vitamin D metabolic features in women of reproductive age presenting with abnormal uterine bleeding and associated extragenital conditions.

MATERIALS AND METHODS

The study was conducted at the Department of Obstetrics, Gynecology, Pediatric Gynecology and Medical Genetics of KhNMU (clinical base Municipal Non-profit Enterprise "Professor O. I. Meshchaninov City Clinical Hospital of Emergency and Intensive Medical Care" of Kharkiv City Council). The study included 110 women of reproductive age, divided into two clinical groups. The first group (main group, MG) comprised 80 patients with AUB accompanied by extragenital conditions (ECs). The second group (control group, CG) consisted of 30 somatically healthy women who attended scheduled preventive examinations.

Women in the MG received inpatient treatment in the gynecological department of the medical institution. All participants provided written informed consent for the use of their data in scientific research, in accordance with the ethical principles outlined in the latest edition of the Declaration of Helsinki by the World Medical Association.

Exclusion criteria included pregnancy (as a potential cause of uterine bleeding), decompensated somatic diseases, cancer, and ongoing hormone therapy at the time of examination. All women underwent thorough evaluation using comprehensive clinical and laboratory methods.

In assessing the hormonal status of women in both the MG and CG, serum concentrations of luteinizing hormone (LH), follicle-stimulating hormone (FSH), progesterone (PRG), and estradiol (E2) were measured by enzyme-linked immunosorbent assay (ELISA) using standard test kits from Biointernational, France.

Serum 25-hydroxyvitamin D (25-OH)D, vitamin D) was determined by competitive ELISA with a luminescent reagent (Siemens Healthcare Diagnostics, Germany) on an Atellica IM 1600 analyzer (Germany).

Statistical data processing was performed using the general-purpose software package Statistica 6.0, applying contingency tables and Pearson's chi-square (χ^2) test.

FRAMEWORK

The study was conducted within the framework of the research project "Optimization of Clinical, Diagnostic, and Therapeutic Approaches to Managing Gynecologi-

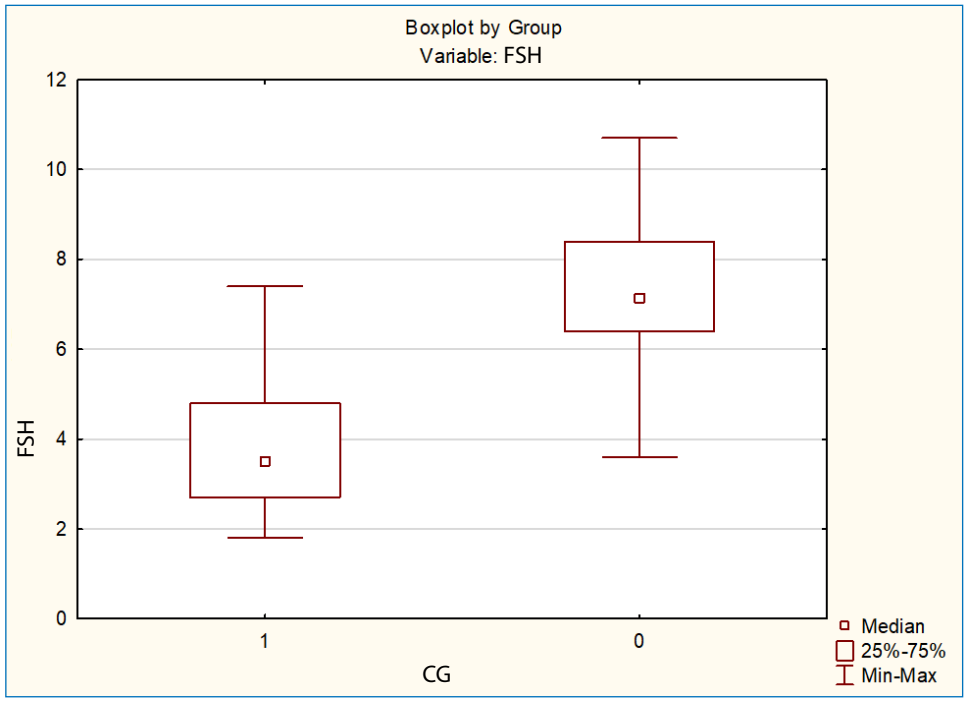

Fig. 1. Serum FSH levels in women from the MG and Contr.G (mIU/mL), 1 – MG, 0 – Contr.G
Picture taken by the authors

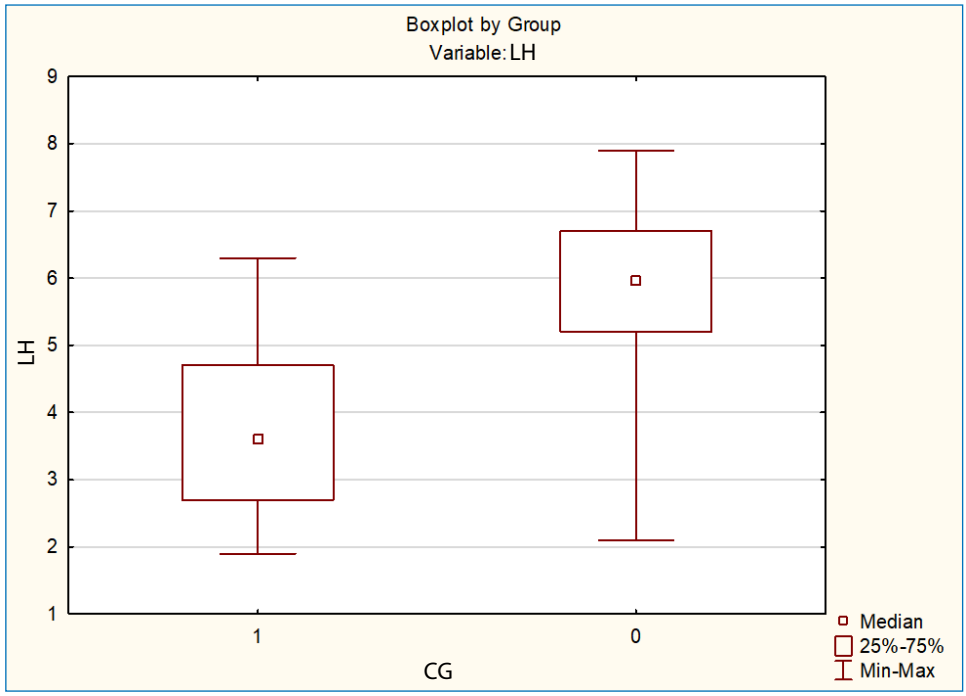

Fig. 2. Serum LH levels in women from the MG and Contr.G (mIU/mL), 1 – MG, 0 – Contr.G
Picture taken by the authors

cal Patients Considering Age and the Presence of Extragenital Conditions", registration number 0122U000257.

RESULTS

The study examined women with a mean age of 31.5 ± 13.5 years. The most common ECs identified were diseases of the endocrine, circulatory, and digestive systems. Within these, endocrine disorders predominated, with obesity accounting for 75% and thyroid disorders for 17.5%. Digestive system diseases, primarily chronic gastritis, were present in 16.25% of cases, while cardiovascular conditions such as hypertensive disease were found in 15%. Among the patients with AUB, 41.25% had two or more concurrent somatic diseases. Specifically, 9 patients (11.25%) presented with both hypertensive disease and obesity; 4 patients (5%) had obesity combined with varicose veins; 9 patients (11.25%) had neurocirculatory dystonia alongside chronic gastritis; 8 patients (10%) suffered from obesity and type II diabetes mellitus; and 3 patients (3.75%) exhibited chronic gastritis with obesity.

Discriminant analysis of the variables, conducted using the Kruskal–Wallis rank test (KWT), demonstrated

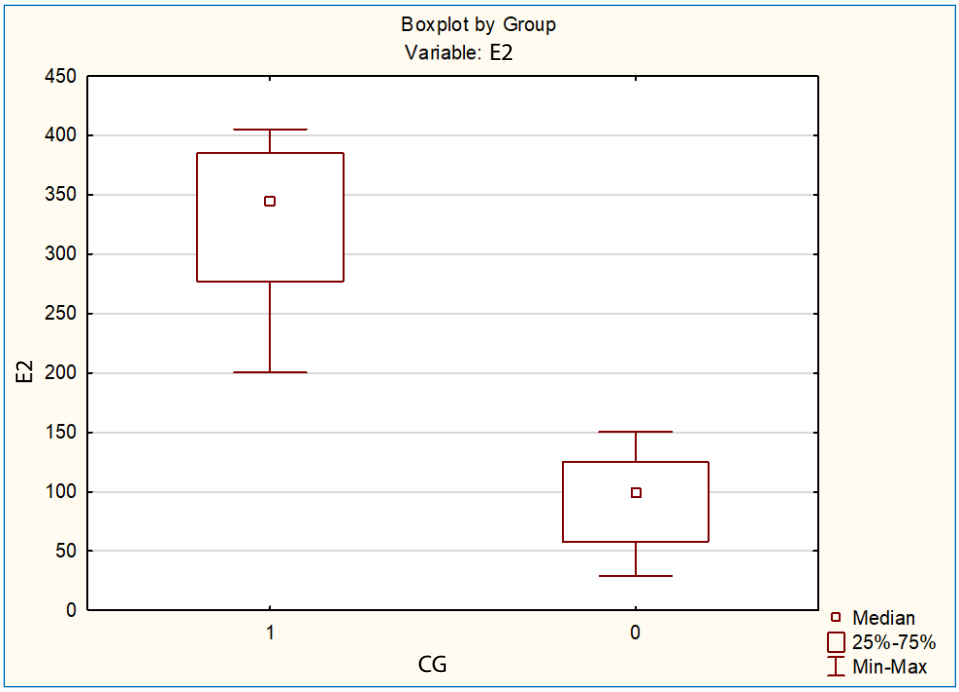

Fig. 3. Serum E2 levels in women from the MG and Contr.G (pg/mL), 1 – MG, 0 – Contr.G
Picture taken by the authors

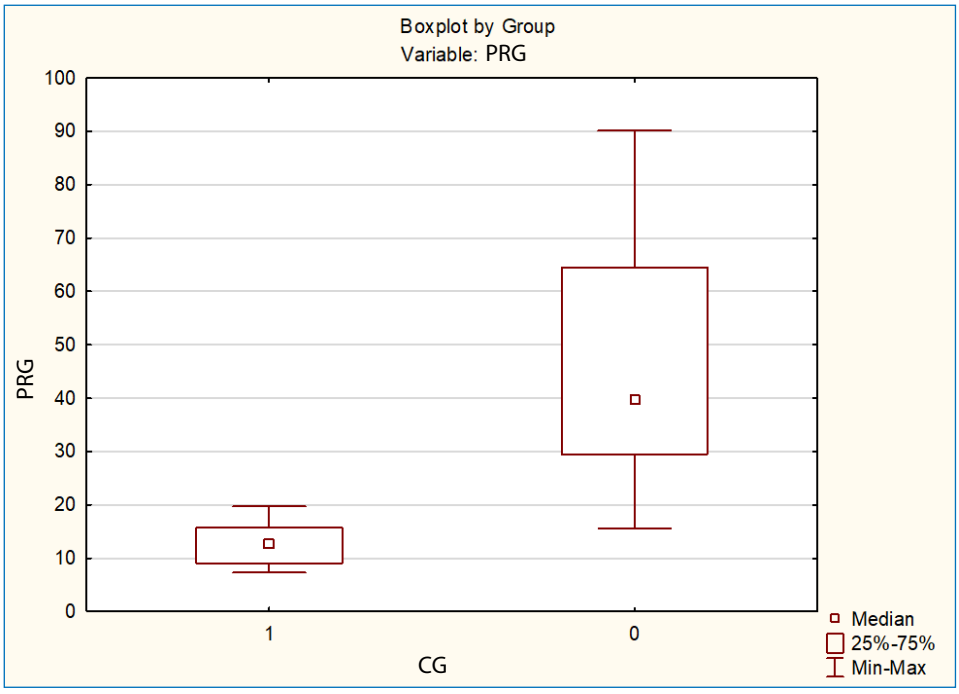

Fig. 4. Serum PRG levels in women from the MG and Contr.G (nmol/L), 1 – MG, 0 – Contr.G
Picture taken by the authors

a statistically significant dependence of all measured parameters on the group. This finding supports the relevance and potential informativeness of comparing these indicators across the groups.

In patients from the MG, the interquartile range of serum FSH levels was 1.97 ÷ 7.59, with a median value of 3.89. In the CG, the interquartile range was 3.60 ÷ 10.70, with a median value of 7.15 (Fig. 1).

Data on serum LH levels in women from the MG and CG are presented in Fig. 2.

In patients from the MG, the interquartile range of serum LH levels was 1.99 ÷ 6.30, with a median value of 3.62. In the CG, the interquartile range was 2.10 ÷ 8.94, with a median value of 6.05.

Data on serum E2 levels in women from the MG and CG are presented in Fig. 3.

In patients from the MG, the interquartile range of serum E2 levels was 200.07 ÷ 410.15, with a median value of 349.10. In the CG, the interquartile range was 28.90 ÷ 150.30, with a median value of 99.10.

Data on serum PRG levels in women from the MG and CG are presented in Fig. 4.

In patients from the MG, the interquartile range of serum PRG levels was 8.99 ÷ 19.98, with a median value of 14.82. In the CG, the interquartile range was 15.60 ÷ 90.10, with a median value of 39.75.

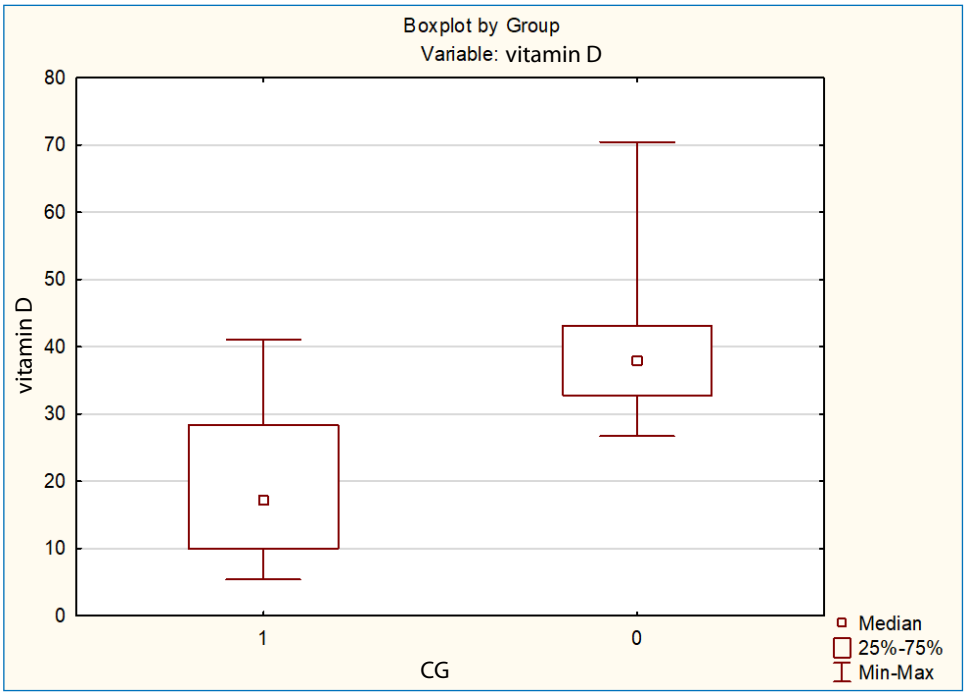

Fig. 5. Serum vitamin D levels in women from the MG and Contr.G (ng/ml), 1 – MG, 0 – Contr.G
Picture taken by the authors

Data on serum vitamin D levels in women from the MG and CG are presented in Fig. 5.

In patients from the MG, the interquartile range of serum vitamin D levels was 6.15 ÷ 40.78, with a median value of 16.80. In the CG, the interquartile range was 26.70 ÷ 70.40, with a median value of 37.85.

DISCUSSION

The obtained data show that the mean values, medians, and interquartile ranges of serum FSH, LH, PRG, and vitamin D levels were generally lower in MG patients compared to those in the CG.

Effective diagnosis of conditions causing AUB is based on the systematic evaluation of all potential contributing factors. Diagnostic methods used in the examination of such patients typically include the assessment of hormone concentrations such as E2, PRG, FSH, LH, among others. The need for these tests is individualized and primarily determined by the specific clinical status of the patient.

Laboratory findings demonstrated decreased serum concentrations of the following hormones in MG patients compared to CG: FSH by 1.84 times (Fig. 1), (KWT, $p < 0.01$); LH by 1.67 times (Fig. 2), (KWT, $p < 0.01$); PRG by 2.68 times (Fig. 4), (KWT, $p < 0.01$). Serum vitamin D levels in the MG were also reduced by 2.25 times compared to the CG (Fig. 5), (KWT, $p < 0.01$).

Serum E2 levels in women from the MG were significantly higher than those in the CG, with elevated mean values, medians, and interquartile ranges. Specifically, serum E2 levels in the MG were 3.52 times higher compared to the CG (Fig. 3), (KWT, $p < 0.01$).

All women in the MG exhibited hyperestrogenism. Both absolute and relative hyperestrogenism are commonly associated with the development of non-atypical endometrial hyperplasia. Several mechanisms may contribute to this condition. A decrease in serum sex hormone-binding globulin (SHBG) leads to increased levels of free estrogens in plasma. In metabolic disorders such as hyperinsulinemia, insulin resistance, and obesity, E2 is synthesized in adipose tissue due to reduced SHBG production by the liver. This hormonal background is particularly unfavorable for sufficient PRG synthesis during the second phase of the menstrual cycle [23].

In total, 60 women (75%) from the MG were overweight or obese, which indicates a high prevalence of metabolic disturbances. These findings confirm the statistically significant increase in serum E2 levels in MG patients (KWT, $p < 0.01$).

PRG also plays a key role in endometrial disorders in reproductive-age women. Understanding its role is essential in addressing clinical challenges related to the treatment and prevention of hyperplastic and proliferative disorders such as endometriosis and uterine fibroids. Elevated E2 levels alone may not support adequate PRG synthesis in the luteal phase.

Moreover, PRG deficiency can impair estradiol synthesis. E2 regulates endometrial proliferation, including the receptor-mediated actions of PRG [24]. Inadequate activation of PRG receptors often results from insufficient estrogen levels. Without the balanced action of both estrogen and progesterone, physiological endometrial transformation cannot occur. Even when PRG levels are adequate, low E2 concentrations or altered receptor sensitivity may lead to morphological immaturity of the

endometrium. Therefore, not only hormone levels but also the integrity of all mechanisms involved in their biological activity are essential for reproductive health [25].

Over the past decade, a growing number of researchers have investigated the functions of vitamin D, its effects on the functioning of various organs and systems, and its role in the development of pathological processes [26].

MC disorders among women of reproductive age remain a significant societal issue, while vitamin D deficiency is highly prevalent. Singh V et al. (2021), in their study, identified that optimal serum levels of vitamin D play a role in folliculogenesis, normal ovulatory function, and menstrual regularity. The study aimed to explore the potential association between vitamin D deficiency and MC disturbances. Given that vitamin D is inexpensive, widely accessible, and has minimal side effects, the authors suggested it may be recommended for women with menstrual irregularities [27].

In a separate study, Jukic AMZ et al. (2018) concluded that vitamin D levels may influence MC length through their association with a prolonged follicular phase due to delayed ovulation [17].

More recently, Muthukumaran D et al. (2025) emphasized the essential role of vitamin D in maintaining menstrual health and its broad impact on women's reproductive well-being. Summarizing their findings, the authors highlighted a complex relationship between vitamin D levels and MC regulation, hormonal balance, and reproductive function. In particular, vitamin D deficiency is common and may exacerbate menstrual disorders such as dysmenorrhea and menorrhagia [28].

The study revealed a statistically significant correlation ($p < 0.05$) between serum levels of E2 and vitamin D in the examined groups of patients ($r = 0.61$).

In the MG, hyperestrogenism was accompanied by a deficiency in the luteal (second) phase of the menstrual cycle. The observed correlation between E2 and vitamin D levels indicates metabolic disturbances in these women, with 75% of MG patients suffering from obesity, which contributes to additional estrogen synthesis in adipose tissue alongside vitamin D deficiency in serum

CONCLUSIONS

This study revealed distinct features of the hormonal profile and vitamin D metabolism in women of reproductive age with abnormal uterine bleeding and concomitant extragenital conditions. Notably, these patients exhibited decreased levels of LH, FSH, PRG, and vitamin D amid hyperestrogenemia. Furthermore, a correlation was found between E2 and vitamin D levels in the blood serum.

PROSPECTS FOR DEVELOPMENT

Effective identification of the causes of AUB relies on a systematic investigation of all potential etiological factors. Diagnostic methods used during the examination of patients with AUB include, in particular, the assessment of hormone levels such as E2, PRG, FSH, LH, as well as vitamin D. The necessity for these tests is determined individually, primarily depending on the specific condition of each patient. All of the above will contribute in the future to optimizing reproductive system function and reducing the risk of emergency complications in this group of women.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Liudmyla A. Vygivska
Kharkiv National Medical University
4 Nauky Avenue, 61022 Kharkiv, Ukraine
e-mail:liudmilavygovskaya@gmail.com

ORCID AND CONTRIBUTIONSHIP
Liudmyla A. Vygivska: 0000-0002-9389-4845 A D F
Roman Ye. Blahoveshchenskyi: 0000-0003-3022-8180 B F
Yevhen V. Blahoveshchenskyi: 0000-0002-0735-6515 B F
Yevheniya B. Radzischevska: 0000-0001-9149-7689 C
Igor Yu. Rakytianskyi: 0009-0009-5986-6988 A F

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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