DOI: https://doi.org/10.30841/2708-8731.7.2024.315355

Correlation between melatonin and vitamin D3 deficiency in Iraqi female patients with polycystic ovarian syndrome

E. J. Jamel
College of Nursing Science, University of Kirkuk, Kirkuk, Iraq

Polycystic ovary syndrome (PCOS) is the most common hyperandrogenic disorder in women and one of the leading causes of anovulatory infertility. Depletion of vital hormones in the organism, such as in the case of PCOS, has been identified as one factor contributing to poor pregnancy outcomes and associated issues in women. Vitamin D level in PCOS patients regulates fertility through membrane-bound receptors in oocytes, regulating luteinizing hormone (LH), and progesterone surges.
The objective. **To examine the correlation between melatonin and vitamin D3 deficiency in Iraqi pregnant women with PCOS under the age of 40.**
Material and methods. **Two hundred women were recruited for the study and divided into two groups: patients with PCOS (n=100) and healthy females without PCOS (n=100). All participants were administered medical questionnaires, and their body mass index (BMI) was determined. Blood samples from participants were obtained for biochemical analysis to assess follicle-stimulating hormone (FSH), luteinizing hormone (LH), anti-Müllerian hormone (AMH), melatonin, and vitamin D levels.**
Results. **The results revealed that 65% of PCOS patients were between 20 and 30 years old and healthy control persons did not show any variations based on age. Patients with PCOS had significantly ($p<0.001$) higher levels of LH and FSH (1.98±0.07 nmol/mL and 11.15±0.25 mIU/L, respectively) compared with healthy controls (1.06±0.02 nmol/mL and 6.67±0.25 mIU/L, respectively).**
The PCOS group had significantly ($p \le 0.01$) reduced mean vitamin D3 level related to the control group. There was no significant correlation between vitamin D3 and melatonin levels in the PCOS group.
The study showed that BMI was significantly higher in women with PCOS compared to healthy women. The study also found a positive relationship between BMI and AMH concentration, as well as between FSH and vitamin D3 levels in women with PCOS. However, there was no association between vitamin D3 and melatonin or BMI.
Conclusion: **The study found that D3 deficiency is a significant component in female PCOS patients that might be a new biomarker for PCOS in Iraqi women.**
Keywords: *polycystic ovary syndrome, vitamin D3, anti-Müllerian hormone, melatonin.*

Кореляція між дефіцитом мелатоніну та вітаміну D3 у пацієнток із синдромом полікістозних яєчників в Іраку

E. J. Jamel

Синдром полікістозних яєчників (СПКЯ) є найпоширенішим гіперандрогенним розладом у жінок і однією з основних причин безпліддя, пов’язаного з ановуляцією. Недостатність життєво важливих гормонів в організмі, яка відзначається при СПКЯ, визначено як один із факторів, що зумовлює негативні результати вагітності та пов’язані із цим проблеми у жінок. Рівень вітаміну D у пацієнток із СПКЯ регулює фертильність через мембранозв’язані рецептори в ооцитах, регулюючи рівень лютеїнізуючого гормону (ЛГ) і підвищення вмісту прогестерону.
Мета дослідження: вивчення кореляції між мелатоніном і дефіцитом вітаміну D3 у жінок із СПКЯ віком до 40 років в Іраку.
Матеріали та методи. У дослідження увійшли 200 жінок, які були розподілені на дві групи: пацієнтки з СПКЯ (n=100) і здорові жінки без СПКЯ (контрольна група, n=100). В усіх учасниць дослідження проведено медичне анкетування та визначено індекс маси тіла (ІМТ). У крові визначали концентрації фолікулостимулювального гормону (ФСГ), ЛГ, антимюллерова гормону (АМГ), мелатоніну та вітаміну D3.
Результати. Установлено, що 65% пацієнток із СПКЯ були у віці від 20 до 30 років, що не відрізнялось від вікових показників здорових жінок. Пацієнтки з СПКЯ мали значно ($p<0,001$) вищі рівні ЛГ і ФСГ (1,98±0,07 нмоль/мл і 11,15±0,25 мМО/л відповідно) порівняно зі здоровими особами (1,06±0,02 нмоль/мл і 6,67±0,25 мМО/л відповідно).
Група пацієнток із СПКЯ мала значно ($p \le 0,01$) знижену середню концентрацію вітаміну D3 порівняно з контрольною групою. Не було суттєвої кореляції між рівнями вітаміну D3 і мелатоніну у групі СПКЯ.
Дослідження продемонструвало, що ІМТ був значно вищий у жінок із СПКЯ порівняно зі здоровими жінками. Виявлено також позитивний зв’язок між ІМТ та рівнями АМГ, а також між рівнями ФСГ і вітаміну D3 у жінок із СПКЯ. Однак зв’язку між вмістом вітаміну D3 і мелатоніну або ІМТ не виявлено.
Висновки. Отже, установлено, що дефіцит D3 є важливим показником у пацієнток з СПКЯ, який може бути новим біомаркером СПКЯ в іракських жінок.
Ключові слова: *синдром полікістозних яєчників, вітамін D3, антимюллерів гормон, мелатонін.*

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)

Polycystic ovarian syndrome (PCOS) is a common gynaecological illness that mostly affects women and is connected with a variety of chronic health issues. The dangers include hyperandrogenemia, insulin resistance, and obesity, which may have an impact on both pregnancy outcomes and the woman's long-term health. An earlier search strategy revealed a clear relationship between obesity, PCOS, and long-term risks for type 2 diabetes [1].

PCOS is highly prevalent obesity-related comorbidity, that develops in girls and women who are genetically predisposed to its development. PCOS affects between 6–10% of reproductive-age women and often develops in young woman less than 40 [2–5].

While vitamin D insufficiency affects around 67-85% of people with PCOS condition [6]. Vitamin D is required for the maintenance and management of calcium levels in the body, thus, a lack of it raises the risk of developing several chronic diseases. Vitamins are fat-soluble hormones that regulate calcium levels and bone mineralization. Vitamin D exhibits remarkable metabolic and physiological properties. Humans rely on endogenous syntheses, activated by ultraviolet light exposure, to provide approximately 90% of the vitamin D (D2 and D3) required for human metabolic activities [7].

Obesity, PCOS, and pregnancy increase the need for vitamin D. Therefore, vitamin D insufficiency is more common in these populations and may be more severe than in healthy people [8]. Vitamin D receptors are found in both male and female reproductive tissues, cells, and organs, supporting the notion that vitamin D increases fertility. Men's testes, hypophysis, ovaries, endometrium, granulosa cells, placenta, decidua, and spermatogenesis cells all have vitamin D receptors.

Vitamin D receptors are not only in the gut [9], but have been found in the hypothalamic Pit-1 gene promoter. Pit-1 has a role in the development of the front of the pituitary gland and regulates growth hormone and prolactin gene activity. The pituitary gland regulates luteinizing hormone (LH), follicle-stimulating hormone (FSH) receptor, and other ovarian steroid hormone (progesterone, oestradiol, and oestrone) gene expression, as well as follicular maturation and selection. All these are the downstream effects of vitamin D [6], according to human and animal studies [10]. Seasonal fluctuations alter vitamin D and anti-Müllerian hormone (AMH) levels, both of which are markers of ovarian reserve. Winter AMH levels are 18% lower than summer levels [11].

The extent of the decrease in AMH levels reflects the change in pretreatment AMH and vitamin D levels due to the effect of various drugs and treatments on ovarian reserve. Studies have shown that treatments such as oral contraceptives and metformin can lead to a significant reduction in AMH levels [12]. In addition, follicular fluid composition, influenced by vitamin D levels, can affect AMH levels in infertile patients undergoing controlled ovarian hyperstimulation for in vitro fertilization [13].

Therefore, the present study **aimed** to investigate the potential risk associated with the correlation between melatonin and vitamin D deficiency in Iraqi pregnant women under 40 years old with PCOS.

Table 1

The body mass index range

BMI levels (kg/m^2)	Range
18.5 to 24.9	Normal weight
25.0 to 29.9	Over-weight
30 or more	Obesity

BMI: body mass index.

MATERIALS AND METHODS

The study recruited Iraqi women under the age of 40 at the International Hospital in Baghdad/ Iraq between February and December 2022. Two hundred women were recruited for the study and divided into two groups: PCOS female patients (N = 100) and healthy control females without PCOS (N = 100) who were included in the control group. (N means number of participants). Polycystic Ovary Syndrome was diagnosed based on the Rotterdam criteria of 2017, which require at least two of the following criteria: irregular ovulation, hyperandrogenism (clinically or biochemically), and polycystic ovaries as seen on ultrasound (14). The duration of Polycystic Ovary Syndrome in the patient group ranged from 1 to 5 years.

The study excluded healthy control subjects with a positive PCOS family history and excessive hair appearance. All participants provided informed consent before completing a medical questionnaire. An aliquot of 5 mL of blood was drawn from the patient's veins and deposited in a centrifuge tube. After coagulation, serum was isolated from the clotted blood cells by centrifugation at 5,000 rpm for 10 minutes. Before processing, the serum was cooled [15]. The blood samples were subjected to biochemical analysis to determine the levels of biochemical markers.

Serum hormone levels were measured using an automated Mini VIDAS device by applying serum samples to the device and then automatically processing them for 15 minutes. The study also estimated the body mass index (BMI). The following formula was used to compute female patients' BMI from estimated weight, and height. Following the World Health Organization's recommendation, BMI was calculated by dividing individuals' weight in kilograms by their height in meters squared [16], as depicted in Table 1.

Human melatonin levels were estimated using the enzyme-linked immunosorbent assay (ELISA). The procedure was carried out as described in reference [17]. Diluted standard, blank, and sample wells were prepared. There were eight wells in total: seven for the test solutions and one empty. An aliquot of 100 μL standard working solution and samples were introduced into each well. Plate sealant was used to seal each plate. The mixture was incubated at 37 °C for 80 minutes. Each well was subjected to water extraction. The aspirated solution was washed in each well for 1–2 minutes with 200 μL of a stronger wash solution. The plate was then placed on absorbent paper to remove any remaining liquid from the wells. A thorough cleaning process was performed three times. After the last washing step, any residual wash buffer was aspirated or decanted, and the plate was dried by blotting.

The plate was gently flipped and tapped in the opposite direction with a fresh, absorbent paper. The wells were then rinsed five times with 300 μL of wash buffer before being sealed with the plate sealer. Each well was then filled with 100 μL of biotinylated-antibody working solution and incubated for 50 minutes at 37 °C.

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)

The solution was then removed and washed three times, as previously mentioned. An aliquot of 100 μL of streptavidin-HRP working solution was added to each well. The plate was covered and incubated at 37 °C for 50 minutes. Then it was aspirated and washed five times. All wells were treated with 90 mL of TMB (3,3',5,5'-Tetramethylbenzidine) substrate solution. A fresh plate sealer was pre-warmed at 37 °C for 20 minutes.

This caused the TMB substrate solution liquid to appear blue. Fifteen minutes later, the optical density (OD) was measured with a microplate reader at 450 nm wavelength. An aliquot of 50 μL of stop solution was added to each well until the solution turned yellow. The plate side was gently tapped to mix the liquid. TMB substrate solution and stop reagent were added to the well sequentially. The bottom of the plate was then wiped and cleaned so that the water droplets and fingerprints did not leave bubbles in the liquid. For calculations relating to the ELISA procedure, a reader device (human company/Germany) was used for the estimation of absorbance (abs), concentration (conc.), linear equations, and cut-off values.

The competition principle was employed in the present investigation to determine vitamin D levels. The procedure involved three incubation steps [17]. Reagents 1 and 2 were used to dissolve 25-hydroxyvitamin D from the VDBP (Vitamin D binding protein) in a pretreatment step of a 20 mL sample. The preparation was incubated. Then, a pretreatment sample was added to the ruthenylated VDBP conjugate, which led to a chemical reaction during the second incubation.

An antibody against 25-dihydroxyvitamin D can bind to the sample and react in the absence of an antibody. In the third incubation step, unbound ruthenylated vitamin D binding proteins compete with stabilized streptavidin-coated microparticles and biotin-tagged 25-hydroxyvitamin D for binding to the solid phase turntable (streptavidin/biotin) in the presence of 25-hydroxyvitamin D. The reactant mixture was introduced into the measurement chamber. Minuscule foreign granules were arranged in place by the magnetic force of the electrode.

ProCell/ProCell M is an extractor with powerful extraction technology that can produce a wide range of compounds without restriction. A photomultiplier was used to detect chemiluminescence from electrodes at a potential.

The Statistical Analysis System program was used to analyze all the data, and the data were expressed as mean ± SD. Significant statistical comparisons between groups were identified using the t-test, with a p-value of <0.01 or 0.05, indicating significance.

RESULTS AND DISCUSSION

Table 2 shows the demographic distribution of the study groups. The results revealed that 65% of PCOS patients were between the ages of 20 and 30. Also, 60% of PCOS patients had a positive family history, and 70% had excessive or heavy hair. Healthy control groups did not show any variations based on age. Most PCOS patients were under 40 years old (65%), had a positive family history (60%), and had hirsutism (70%). As a result, PCOS is most likely caused by the complicated interactions of various factors, including age and family history. Women with PCOS are more likely to acquire unattractive facial hair.

Polycystic ovarian syndrome is characterized by a variety of symptoms, including hormonal imbalance, the presence of ovarian cysts, irregular menstrual cycles, hormonal acne, insulin resistance, infertility, excess body hair, and hair loss. This is because it raises the levels of androgen hormones, which induce these symptoms and considered as common causes of infertility [18, 19]. The PCOS group had significantly (p≤0.01) reduced mean vitamin D levels compared to the control group (Table 4). Another study found that 93.1% of PCOS patients had low serum vitamin D levels (<20 ng/mL) compared to healthy control groups, which was consistent with previous findings [20].

The study also discovered a significant increase in blood LH levels and a drop in serum FSH levels in PCOS patients compared with healthy female controls. Women with PCOS suffer abnormalities in the intact gonadotropin axis, which appear to result in increased LH secretion and decreased FSH secretion [21]. While other studies showed that there is a higher serum vitamin D level in the control group than in PCOS patients, which was statistically significant (P<0.001) [22].

A statistical study utilizing the student's T-test revealed that BMI among PCOS participants was significantly (p≤0.01) higher than the control group of healthy adults. When considering fertility in women with PCOS, one of the most essential characteristics to consider is BMI. The study also found no correlation between BMI and both LH and FSH. These findings of agreed with recent studies which showed that moderate or less significant correlational relationships between BMI and the LH/FSH ratio. It has also been discovered that BMI is inversely correlated with FSH in obese women [21].

Furthermore, they reported a higher prevalence of hirsutism in obese women than in slim women [21]. The results displayed in Table 3 demonstrated that LH levels were significantly lower in PCOS patients compared to healthy female controls. However, the results in Table 3 highlighted a significant (p≤0.01) decrease in FSH in PCOS patients compared to the control group.

Serum vitamin D levels were determined in the present study, and the results (Table 4) revealed a significant (p≤0.01) decrease in serum vitamin D levels in PCOS

Table 2

Demographic distribution in patients and healthy control groups

Groups	Age		Family history		Heavy hair appearance	
	20–30 years old	30–40 years old	Positive	Negative	Positive	Negative
Female with PCOS (n=100)	65 (65.00%)	35 (35.00%)	60 (60.00%)	40 (40.00%)	70 (70.00%)	30 (30.00%)
Healthy female control (n=100)	50 (50.00%)	50 (50.00%)	0 (0.00%)	100 (100%)	0 (0.00%)	100 (100%)
Chi-Square: χ^2 (P-value)	0.0419 *		0.0001 **		0.0001 **	

Notes: * – Significant at (p≤0.05); ** – Significant at (p≤0.01); PCOS: polycystic ovarian syndrome.

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)

Table 3

Determination of LH, FSH, and AMH hormone level in Iraqi females with and without polycystic ovarian syndrome groups

Groups	LH µU/ml	FSH U/L	Vitamin D (ng/dl)
Female with PCOS (n=100)	1.49±0.04	6.93±6.93	22.82±1.53
Healthy female control (n=100)	2.20±0.12	8.89±0.18	26.59±0.94
T-test (P-value)	0.212 ** (0.0001)	0.293 ** (0.0001)	4.949 ** (0.0001)

Note: ** – Significant at (p≤0.01).

Table 4

Determination of vitamin D, body mass index, and melatonin hormone in Iraqi female groups with and without polycystic ovarian syndrome

Groups	Vitamin D (ng/dl)	Melatonin (mg/dl)	BMI (kg/m²)
Female with PCOS (n=100)	22.82±1.53	1.31±0.20	35.81±6.48
Healthy female control (n=100)	26.59±0.94	5.39±1.85	32.96±1.72
T-test (P-value)	4.949 ** (0.0001)	2.658 ** (0.0030)	5.208 0.319

Note: ** – Significant at (p≤0.01).

patients compared to the control group. Generally, these findings showed that the levels of AMH in PCOS patients were not significantly higher than in the control group. In women with PCOS, the correlation coefficient (R) between BMI and AMH levels was zero.

Melatonin levels were significantly lower in PCOS patients than in the control group, with a confidence limit threshold of ≤0.01. Localization of melatonin receptors in particular areas of the ovary and intrafollicular fluid shows that melatonin might modulate sex hormonal agent secretion during ovarian follicular development. Melatonin acts as an antioxidant and free radical scavenger, shielding the follicles from oxidative stress and avoiding apoptosis or atresia. The process enhances the developmental growth of the follicles and also assists the ovary in releasing eggs [24]. Another study also found no significant relationship between vitamin D and melatonin in women with PCOS.

There was a significant increase (p≤0.01) in BMI in PCOS patients compared to the healthy control group (Table 5). The correlation coefficient in PCOS female patients (Table 4) showed a positive correlation between BMI and AMH levels, as well as a positive proportional correlation between FSH and vitamin D. The results also showed that there was no significant correlation between vitamin D and melatonin, as well as between vitamin D and BMI.

The correlation coefficient analysis displays a positive association between vitamin D and FSH in the PCOS cases, indicating a good fit between two important markers. It also found a significant increase in vitamin D level in PCOS women than in age- and BMI-matched control women [24–27]. It agreed that vitamin D had crucial effect on PCOS in women [28, 29].

It also demonstrated that vitamin D deficiency in PCOS women was correlated with metabolic risk factors, including vitamin D insufficiency, low High-Density Lipoprotein-C levels, and insulin resistance independent of obesity measures [30, 31]. Thus, it can be inferred that vitamin D deficiency is more prevalent in both ethnic groups.

CONCLUSIONS

Younger women and those with a family history are more likely to have PCOS. Many PCOS patients experience hirsutism. The study found that PCOS women have significantly lower vitamin D levels than healthy women. Vitamin D de-

Table 5

Correlation coefficient between difference variables in patient groups

Female with PCOS		FSH U/L	LH µU/ml	AMH ng/ml	Vitamin D (ng/dl)	BMI (kg/m²)	Melatonin (mg/dl)
FSH U/L	Pearson Correlation	-	0.33 **	0.27 *	0.31 *	-0.04 NS	-0.25 NS
	p-value	-	0.0089	0.036	0.0154	0.725	0.0532
LH µU/ml	Pearson Correlation	-	-	-0.16 NS	0.06 NS	-0.08 NS	0.02 NS
	p-value	-	-	0.201	0.689	0.558	0.987
AMH ng/ml	Pearson Correlation	-	-	-	0.12 NS	0.27 *	-0.16 NS
	p-value	-	-	-	0.334	0.036	0.201
Vitamin D (ng/dl)	Pearson Correlation	-	-	-	-	0.02 NS	0.06 NS
	p-value	-	-	-	-	0.987	0.689
BMI (kg/m²)	Pearson Correlation	-	-	-	-	-	-0.08 NS
	p-value	-	-	-	-	-	0.558

Notes: * – Correlation is significant at the 0.05 level (2-tailed); ** – Correlation is significant at the 0.01 level (2-tailed).

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)

ficiency may contribute to PCOS in people of all ethnicities. Patients with PCOS have elevated LH and low FSH. Infertility, ovarian cysts, and irregular menstruation can arise from PCOS hormone abnormalities. A positive correlation was found between vitamin D and FSH in PCOS patients. Melatonin and vitamin D were unrelated in PCOS women.

Finally, PCOS patients had far lower melatonin levels than controls. The study concluded that vitamin D deficiency, melatonin, hormonal imbalances, and obesity contribute to PCOS. These findings advance our understanding of PCOS and may influence future research and treatment options.

Information about the author

Jamel Essmat Jamal – Assistant Professor, College of Nursing Science, University of Kirkuk, Kirkuk, Iraq; tel.: 009647701305086. *E-mail: dresmat.j.j@gmail.com*

ORCID: 0009-0009-2489-0224

REFERENCES

1. Boomsma CM, Eijkemans MJ, Hughes EG, Visser GH, Fauser BC, Macklon NS. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. Hum Reprod Update. 2006;12(6):673-83. doi: 10.1093/humupd/dml036.
2. Walley AJ, Blakemore AI, Froguel P. Genetics of obesity and the prediction of risk for health. Hum Mol Genet. 2006;15(2):124-30. doi: 10.1093/hmg/ddl215.
3. Vink JM, Sadrzadeh S, Lambalk CB, Boomsma DI. Heritability of polycystic ovary syndrome in a Dutch twin-family study. J Clin Endocrinol Metab. 2006;91(6):2100-4. doi: 10.1210/jc.2005-1494.
4. Franks S. Polycystic ovary syndrome. N Engl J Med. 1995;333(13):853-61. doi: 10.1056/NEJM199509283331307.
5. Barber TM, Franks S. Genetics of polycystic ovary syndrome. Front Horm Res. 2013;40:28-39. doi: 10.1159/000341682.
6. Thomson RL, Spedding S, Buckley JD. Vitamin D in the aetiology and management of polycystic ovary syndrome. Clin Endocrinol (Oxf). 2012;77(3):343-50. doi: 10.1111/j.1365-2265.2012.04434.x.
7. Al-Horani H, Abu Dayyih W, Mallah E, Hamad M, Mima M, Awad R, et al. Nationality, Gender, Age, and Body Mass Index Influences on Vitamin D Concentration among Elderly Patients and Young Iraqi and Jordanian in Jordan. Biochem Res Int. 2016;2016:8920503. doi: 10.1155/2016/8920503.
8. Takács I, Dank M, Majnik J, Nagy G, Szabó A, Szabó B, et al. Hungarian consensus recommendation on the role of vitamin D in disease prevention and treatment. Orv Hetil. 2022;163(15):575-84. doi: 10.1556/650.2022.32463.
9. Menichini D, Facchinetti F. Effects of vitamin D supplementation in women with polycystic ovary syndrome: a review. Gynecol Endocrinol. 2020;36(1):1-5. doi: 10.1080/09513590.2019.1625881.
10. Nandi A, Sinha N, Ong E, Sonmez H, Poretsky L. Is there a role for vitamin D in human reproduction? Horm Mol Biol Clin Invetig. 2016;25(1):15-28. doi: 10.1515/hmbci-2015-0051.
11. Dennis NA, Houghton LA, Jones GT, van Rij AM, Morgan K, McLennan IS. The level of serum anti-Müllerian hormone correlates with vitamin D status in men and women but not in boys. J Clin Endocrinol Metab. 2012;97(7):2450-5. doi: 10.1210/jc.2012-1213.
12. Yin WW, Huang CC, Chen YR, Yu DQ, Jin M, Feng C. The effect of medication on serum anti-müllerian hormone (AMH) levels in women of reproductive age: a meta-analysis. BMC Endocrine Disorders. 2022;22(1):158. doi: 10.1186/s12902-022-01065-9.
13. Bednarska-Czerwińska A, Olszak-Wąsik K, Olejek A, Czerwiński M, Tukiendorf AA. Vitamin D and Anti-Müllerian Hormone Levels in Infertility Treatment: The Change-Point Problem. Nutrients. 2019;11(5):1053. doi: 10.3390/nu11051053.
14. Wang R, Mol BW. The Rotterdam criteria for polycystic ovary syndrome: evidence-based criteria? Hum Reprod. 2017;32(2):261-4. doi: 10.1093/humrep/dew287.
15. Khalaf ZA. Detection of FOXP3 and IL-10 gene expression and immunological biomarkers in Iraqi hyperthyroidism patients treated with radioiodine. Iraq: College of Biotechnology, AL-Nahrain University; 2020. 231 p.
16. Cary N. Statistical analysis system, User's guide. Statistical. Version 9. USA: SAS. Inst. Inc.; 2012. 13 p.
17. Swadi AA, Hilal NN, Abdul-Aziz MM. The role of CRP and BODY MASS INDEX (BMI) in Iraqi premenopausal women osteoarthritis patients. South Asian Res J Pharm Sci. 2023;5(3):81-6.
18. Islam S, Nabi N, Khushbu SA, Ria NJ, Masum AKM. A process of finding common symptoms and diagnosis age among PCOS patients through a survey. In: 12th International Conference on Computing Communication and Networking Technologies (ICCCNT); 2021 July 6-8, Kharagpur. Kharagpur: Kharagpur: Institute of Electrical and Electronics Engineers (IEEE); 2021, p. 1-7. doi: 10.1109/ICCCNT51525.2021.9580114.
19. Zehra B, Khursheed AA. Polycystic ovarian syndrome: symptoms, treatment and diagnosis: a review. J Pharmacognosy Phytochemistry. 2018;7(6):875-80.
20. Lal L, Bharti A, Perween A. To study the status of LH:FSH ratio in obese and non-obese patients of polycystic ovarian syndrome. IOSR J Dent Med Sci. 2017;16(01):20-3. doi: 10.9790/0853-1601012023.
21. Alnakash AH, Al-Tae' NK. Polycystic ovarian syndrome: the correlation between the LH/FSH ratio and disease manifestations. Middle East Fertil Soc J. 2007;12(1):35-40.
22. Eftekhar M, Mirhashemi ES, Molaei B, Pourmasumi S. Is there any association between vitamin D levels and polycystic ovary syndrome (PCOS) phenotypes? Arch Endocrinol Metab. 2020;64(1):11-6. doi: 10.20945/2359-3997000000177.
23. Mahmoudi T, Gourabi H, Ashrafi M, Yazdi RS, Ezabadi Z. Calciotropic hormones, insulin resistance, and the polycystic ovary syndrome. Fertil Steril. 2010;93(4):1208-14. doi: 10.1016/j.fertnstert.2008.11.031.
24. Tamura H, Takasaki A, Taketani T, Tanabe M, Kizuka F, Lee L, et al. The role of melatonin as an antioxidant in the follicle. J Ovarian Res. 2012;(5):5. doi: 10.1186/1757-2215-5-5.
25. Li HW, Brereton RE, Anderson RA, Wallace AM, Ho CK. Vitamin D deficiency is common and associated with metabolic risk factors in patients with polycystic ovary syndrome. Metabolism. 2011;60(10):1475-81. doi: 10.1016/j.metabol.2011.03.002.
26. Pakharenko L, Zhylka N, Shcherbinska O, Kravchuk I, Lasytchuk O, Zhurakivskyi V, et al. The modern pathogenetic challenges of polycystic ovary syndrome. Reprod Health Woman. 2024;(2):75-80. doi: 10.30841/2708-8731.2.2024.304662.
27. Syusyuka V, Sergienko M, Makurina G, Yershova O, Chornenka A. Polycystic ovary syndrome: clinical and pathogenetic aspects of a multidisciplinary problem. Reprod Health Women. 2021;(2):7-14. doi: 10.30841/2708-8731.2.2021.232513.
28. Kim JJ, Choi YM, Chae SJ, Hwang KR, Yoon SH, Kim MJ, et al. Vitamin D deficiency in women with polycystic ovary syndrome. Clin Exp Reprod Med. 2014;41(2):80-5. doi: 10.5653/cerm.2014.41.2.80.
29. Mohylnytska L. The level of adhesion molecules in polycystic ovary syndrome. Reprod Health Woman. 2021;(2):57-63. doi: 10.30841/2708-8731.2.2021.232555.
30. Li HW, Brereton RE, Anderson RA, Wallace AM, Ho CK. Vitamin D deficiency is common and associated with metabolic risk factors in patients with polycystic ovary syndrome. Metabolism. 2011;60(10):1475-81. doi: 10.1016/j.metabol.2011.03.002.
31. Korchinskaya O, Khasha I, Shumilina T. Modern views on the metabolic aspects of polycystic ovary syndrome. Reprod Health Woman. 2023;(8):64-71. doi: 10.30841/2708-8731.8.2023.297796.

Стаття надійшла до редакції 18.07.2024. – Дата першого рішення 24.07.2024. – Стаття подана до друку 28.08.2024

ISSN 2708-8723 (print)
ISSN 2708-8731 (online)