

How to Cite:

Al-Zubaidi, E. M. A., & Alsamarai, A. T. S. (2022). Evaluation of the relationship between vitamin D3 level and sex hormones in women with PCOS. *International Journal of Health Sciences*, 6(S9), 1105–1114. <https://doi.org/10.53730/ijhs.v6nS9.12419>

Evaluation of the relationship between vitamin D3 level and sex hormones in women with PCOS

Enas Malik Ahmed Al-Zubaidi

Department of chemistry, College of education, University of Samarra, Iraq
Email: us4010520003@uosamarra.edu.iq

Abdulsalam Tawfeeq Salih Alsamarai

Department of applied chemistry, College of applied science, University of Samarra, Iraq
Email: salam.t10@uosamarra.edu.iq

Abstract---The current study included collection of 90 serum samples to assess the relationship between the level of vitamin D3 and some biochemical variables in women with polycystic ovarian syndrome. The samples were collected from external laboratories in Salah al-Din Governorate for the period from 10/29/2021 to 12/25/2021. 60 samples were taken for women with PCOS, and 30 samples were taken from the control group, their ages ranged between (18-40) years for healthy women and patients. Vitamin D3 level and some hormones concentrations (luteinizing hormone, follicle-stimulating hormone, and testosterone) were estimated in the blood serum of the study groups. The results of the current study showed that the level of vitamin D3 decreased significantly ($P \leq 0.05$) in women with PCOS compared to healthy women as a control group, the results showed a significant increase ($P \leq 0.05$) in the level of studding hormones (luteinizing hormone, follicle-stimulating hormone, and testosterone) in women with PCOS compared to healthy women as a control group.

Keywords---PCOS, vitamin D3, luteinizing hormone, follicle-stimulating hormone, testosterone.

Introduction

PCOS is one of the most common endocrine and metabolic disorders in premenopausal women. PCOS is defined as heterogeneous disorder, with a combination of signs and symptoms of excess androgen and ovarian dysfunction in the absence of other specific diagnoses. The etiology of this syndrome is still largely unknown, but mounting evidence indicates that suggest that PCOS may be a complex polygenic disorder with strong genetic and environmental

influences, including diet and lifestyle factors. PCOS is often associated with abdominal fat, insulin resistance, obesity, metabolic disorders, and cardiovascular risk factors ⁽¹⁾. More than 1 in 10 women worldwide have PCOS, which is the leading cause of female reproductive and metabolic dysfunction ⁽²⁾. PCOS is believed to be the most common endocrine disorder in women. Common symptoms include irregular menstruation, PCOS, and hirsutism, as well as an increased risk of several conditions, including insulin resistance, dyslipidemia, and infertility ⁽³⁾.

Vitamin D3 is a fat-soluble vitamin ⁽⁴⁾. There are two forms of it, the first form D2 and it is called ergocalciferol. It can be obtained from the raw material ergosterol, a substance found in plants, and it does not have a great nutritional value because it cannot be absorbed through the intestine ⁽⁵⁾. The second form is D3 cholecalciferol, which can be obtained from 7-dehydrocholesterol, which is found in the skin when exposed to sunlight, and can also be obtained from animal foods ⁽⁶⁾. Vitamin D3 is also called the sunshine vitamin because it can be synthesized inside the body from cholesterol when the body is exposed to sunlight ⁽⁷⁾. There are many sources of vitamin D, some natural and some synthetic that can be obtained naturally from food ⁽⁸⁾. It was found that exposure to sunlight is one of the main natural sources for obtaining the vitamin ⁽⁹⁾. While foods rich in vitamin D2 and D3 such as milk, yogurt and vegetable ghee are important industrial sources for obtaining the vitamin ⁽¹⁰⁾.

The ovaries in women with PCOS do not respond to the pituitary hormones appropriately as in the natural ovaries. Both LH and FSH hormones affect the ovaries and their hormones directly, so FSH is the main hormone in the follicular phase of the menstrual cycle if it works to stimulate the formation of the maturation of the eggs and thus the secretion of estrogen from the mature egg ⁽¹¹⁾.

While LH is the main hormone in the luteal phase that stimulates ovulation and then the formation of estrogen and progesterone in the luteal phase after ovulation, and any imbalance in the levels of FSH, LH is reflected in the level of the hormones progesterone and estrogen as well as on the production of the male hormone and thus causes disturbances in the reproduction function of the ovaries, such as the difference in the menstrual cycle, delayed childbearing, or infertility ⁽¹²⁾.

Materials and Methods

The samples

The blood samples were (90) which distributed to two groups, 60 samples were from women with PCOS and 30 blood samples from healthy women as a control group, their ages ranged between (18-40) these samples were collected from external laboratories in Salah El-Din Governorate for the period between 10/29/2021 to 12/2021 \25.

Estimation the level of Vitamin D3

Vitamin D3 was calculated by following the steps attached to the vitamin analysis kit, and according to the instructions of the kit, to estimating the concentration of vitamin D3.

Estimation the concentration of sex hormones

The study included estimation of the levels of sex hormones (luteinizing hormone, follicle-stimulating hormone, and testosterone) by means of an examination kit supplied by the American company Mybiosource by means of the Sandwich enzyme-linked immunosorbent assay (ELISA) technique.

Results and Discussion

The Level of Vitamin D3

The results showed that the mean \pm standard deviation of vitamin D level was (17.063 \pm 3.912) ng/ml for women with PCOS, compared to (35.399 \pm 9.828) ng/ml for healthy women as a control group, as shown in Table (1).

Table (1) the level of vitamin D3 in the blood serum of POC female patients and control group.

Parameter	Mean \pm SD
	Vitamin D ng/ml
Control	35.399 \pm 9.828
Patients	17.063 \pm 3.912
P \leq 0.05	*

Table (1) shows that the level of vitamin D showed a significant decrease (P \leq 0.05) in the blood serum of women with PCOS compared to the control, as shown in Figure (1).

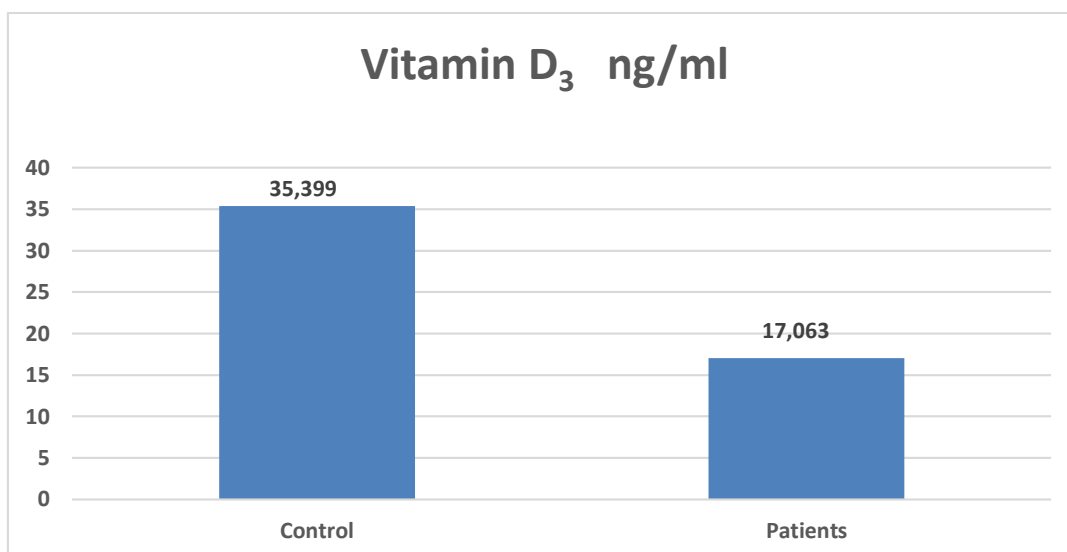


Figure 1 shows the level of Vitamin D₃ in PCOS groups compared to the control group

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of childbearing age with an incidence of 10%, many studies have shown that vitamin D₃ has a positive effect on female reproductive diseases, as well as PCOS, androgen excess and neuroendocrine causes and insulin resistance is all part of the pathophysiology, Some female reproductive organs have been found to contain vitamin D₃ receptors, so vitamin D₃ is essential in the human body ⁽¹³⁾. The results of the current study agree with the results of the study of Ibrahim et al., ⁽¹⁴⁾, which showed a significant decrease in the level of vitamin D₃ in women with PCOS compared to healthy women as a control group. The results of the current study are also in agreement with the results of the study of Li and his group ⁽¹⁵⁾, which showed a decrease in the level of vitamin D₃ among women with PCOS compared with healthy women as a control group.

The reason for the decrease in the level of vitamin D₃ in the current study may be attributed to malnutrition and dependence on fast foods, as well as the poor table for seafood and the lack of interest in health institutions to educate people about the importance of eating foods fortified with vitamin, and the importance of dietary diversity and interest in eating foods rich in vitamin such as egg yolk, beef meat and liver, Milk and cheese, and since the vitamin is one of the fat-soluble vitamins, any factor that affects the absorption of fats in the intestines can affect the absorption of the vitamin, in addition to the way of life in Iraqi society, as the lack of exposure to sunlight within the required peak periods .

The levels of sex hormones

The level of sex hormones, which includes follicle-stimulating hormone, luteinizing hormone and testosterone, was measured in the blood serum of women with polycystic ovary syndrome (PCOS) and healthy women as a control group, and the mean standard deviation of hormones was shown in Table (2).

Table (2) shows the level of FSH, LH, and testosterone in the blood serum of the study groups

Parameter	Mean \pm SD		
	FSH (mIU/ml)	LH (mIU/ml)	Testosterone (mIU/ml)
Control	17.284 \pm 7.972	20.944 \pm 5.899	0.368 \pm 0.106
Patients	22.564 \pm 6.926	24.594 \pm 3.820	0.579 \pm 0.221
P \leq 0.05	*	*	*

***High significant**

The level of follicle-stimulating hormone

The results of the current study showed that the level of FSH hormone was (22.564 \pm 6.926) mIU/cm³ in the blood serum of women with PCOS, while its level was (17.284 \pm 7.972) mIU/cm³ in healthy subjects (control group), as shown in the table (2). It was obtained from the above table that the level of FSH was significantly increased (P \leq 0.05) in women with PCOS compared to healthy subjects as a control group, as shown in Figure (2).

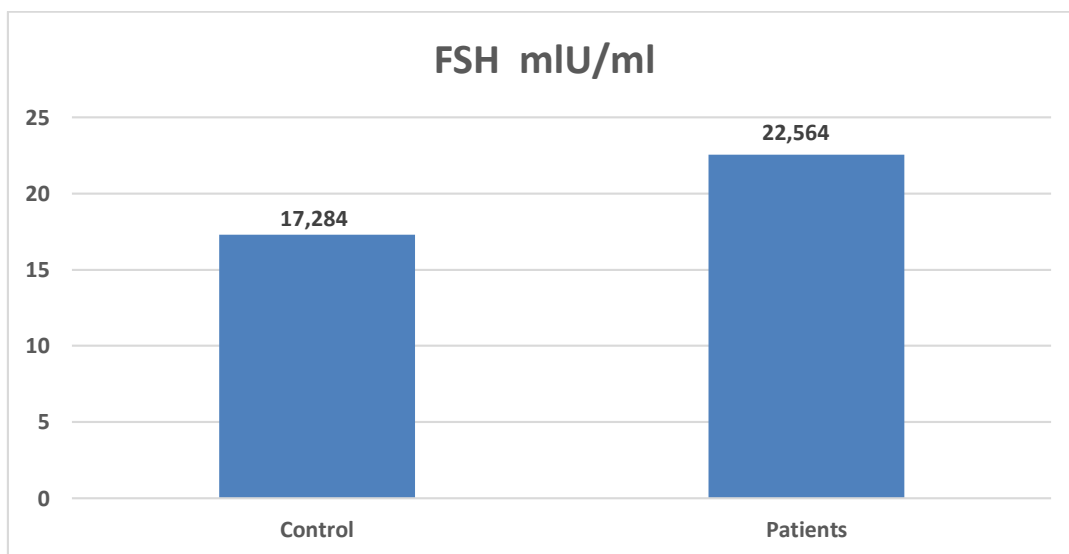


Figure (2) shows the level of FSH in PCOS groups compared to the control group

The results of the current study do not agree with ElSiry et al.,⁽¹⁸⁾ who indicated that the FSH level in the group of women with PCOS was lower than in the control group. Also, the results of the current study did not agree with the results of the study of Al-Tikriti et al.,⁽¹⁹⁾ which they showed no significant differences in the level of FSH in women with PCOS compared with healthy women. The results of the current study agree with the results of the study by Sak et al.,⁽²⁰⁾ which they found high levels of FSH in women with PCOS compared to healthy women as a control group.

The growth of ovarian follicles is under the control of the both hormones FSH and LH, and the response of the ovaries is when the level of FSH reaches the required level, and the level of FSH is variable during the follicular phase, due to the growth of the follicle and sensitivity to the stimulating of the gonadotropins ⁽²¹⁾ . Thus, high levels of sex hormones lead to hormonal disruption and thus the lack of ovulation. The pituitary gland and the hypothalamus are among the main organs that regulate the mechanism of action of the endocrine system ⁽²²⁾. In the anterior lobe of the pituitary gland, the portal system works to produce peptides that bind with specific receptors located on the surfaces of cells, thus either inhibiting hormones or releasing hormones ⁽²³⁾ .

The hypothalamus also stimulates the production of gonadotropins from the pituitary gland through the pulsating production of gonadotropin-releasing hormones, and this leads to the stimulation of genetic transcription of gonadotropins LH and FSH ⁽²⁴⁾ .

Level of serum LH

The results of the current study showed that the level of LH hormone was (24.594 ± 3.820) mIU/cm³ in the blood serum of women with PCOS, while its level was (20.944 ± 5.899) mIU/cm³ in healthy subjects as a control group as shown in the table (2). It is clear from the table (2) that the level of LH was significantly increased, $P \leq 0.05$, in women with PCOS compared to healthy women as a control group, as shown in Figure (3).

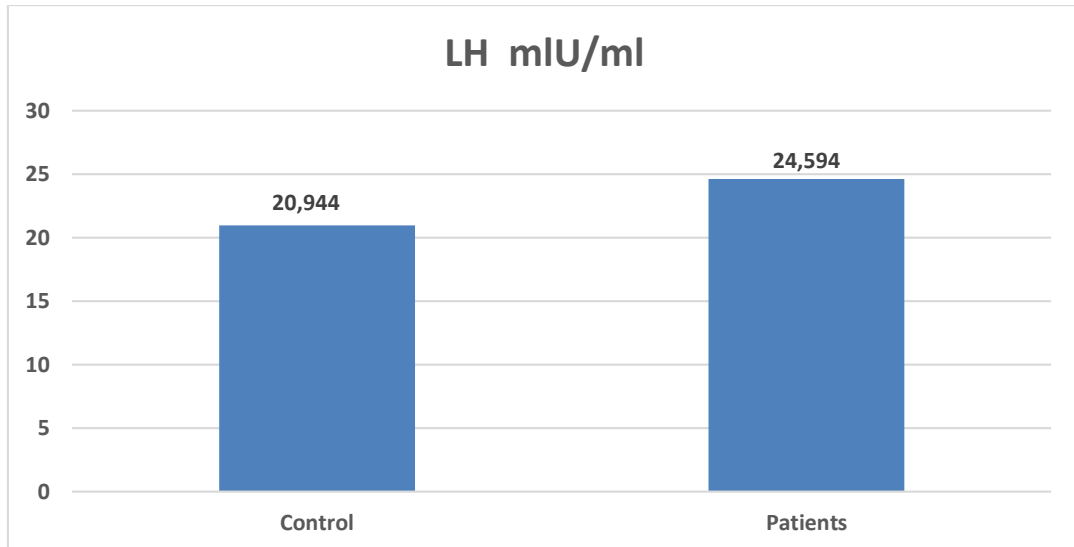


Figure (2) shows the level of LH in PCOS groups compared to the control group

The results of the current study agree with many studies ^(20, 26,25) that showed a significant increase in the level of LH in patients with PCOS. The reason for the high level of the hormone may be due to the increased sensitivity of the pituitary gland to LH-GnR, and this leads to an increase in the concentration of - Gonadotropin-releasing hormones GnRH or to changes in its secretion patterns

(27). So, LH stimulates ovulation and then stimulates the corpus luteum to form steroid hormones (28), but high levels of LH suppress the activity of aromatase and inhibit oocyte growth (29). Thus, the high levels of sex hormones lead to hormonal disruption and thus the lack of ovulation.

Level of serum Testosterone

The results of the current study showed that the level of Testosterone hormone was (0.579 ± 0.221) mIU/cm³ in the blood serum of women with PCOS, while its level was (0.368 ± 0.106) mIU/cm³ of healthy women (control group) as shown in Table (2). The results which obtained from the study indicated that the level of Testosterone was significantly increased ($P \leq 0.05$) among women with PCOS compared to the healthy control group as shown in Figure (4) and table (2).

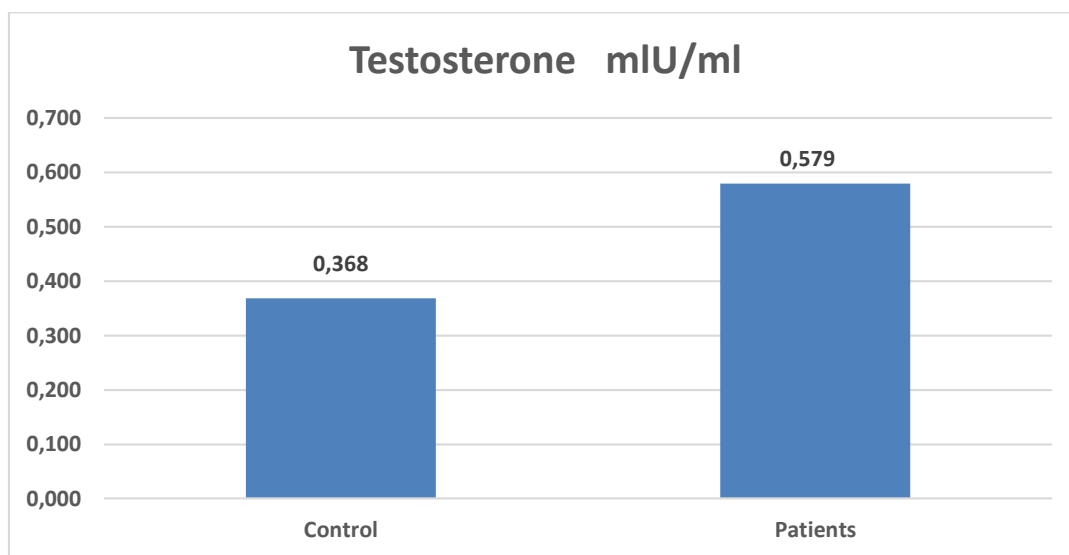


Figure (4) shows the level of testosterone in PCOS groups compared to the control group

The results of the current study agree with the results of several last studies (20, 25, 30) that showed a significant increase in the level of testosterone in women with PCOS compared to healthy women as a control group. Androgens are usually derived from cholesterol in the ovaries and adrenal glands, and can be produced in muscle, liver, skin, and adipose tissue through the conversion of certain types of steroids (31).

In muscle and adipose tissue, a chemical group is added to androgens to turn into estrogens, thus converting testosterone and androstenedion into estrogens, and this agrees with the study of Frhan et al., (32) which showed that the concentration of testosterone hormone of women with PCOS is higher than the control group and that the increase in the concentration of LH hormone results in polycystic ovary syndrome, which causes high testosterone and other hormone disorder.

References

1. Abdallah, A. M., Elazab, G., Mosbeh, M. H., & Sarhan, H. (2021). Role of vitamin D and insulin resistance in polycystic ovary syndrome. *Journal of advanced Biomedical and Pharmaceutical Sciences*, 4(4), 186-194.
2. Abdulwahid, H. H., Hussein, B. A., Omran, Z. S., & Alhasanawy, S. A. (2019). Disorders of sex Hormones and lipid profile in obese and non-obese Women with Polycystic Ovary Syndrome (PCOS) in Karbala City. *Annals of Tropical Medicine and Health*, 22, 100-106.
3. Al-Tikriti, Sherine Bahgat. 2017. The role of hepcidin hormone and some biochemical variables in the sera of patients with polycystic ovary syndrome in Kirkuk. Doctoral thesis, College of Science, Tikrit University (6: 11): 22
4. Arianggara, A. W., Ernawati, E., Handayani, T. P., Sari, F., & Fitria, L. (2022). Relationship of information sources and knowledge with completeness of primigravida's tetanus toxoid immunization. *International Journal of Social Sciences and Humanities*, 6(1), 75-84. <https://doi.org/10.53730/ijssh.v6n1.4738>
5. Bikle, D. Vitamin D metabolism, mechanism of action, and clinical applications. *Chemistry & biology*. 2014;21(3):319-29.
6. Brown, J. B. (1978). Pituitary control of ovarian function—concepts derived from gonadotrophin therapy. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 18(1), 47-54.
7. Conway, G. The Polycystic Ovary Syndrome. Department of Endocrinology. The Middle Sex Hospital Mortimer Street London W1N8AA. January . (2000).
8. Du, C.; Yang, S.; Zhao, X. and Dong, H. Pathogenic roles of alterations in vitamin D and vitamin D receptor in gastric tumorigenesis. *Oncotarget*. 2017;8(17):29474-86.
9. ElSirgany, S., Badawi, H., El-Khayat, Z., Bibers, M., Hamdy, M., Hamdy, A., ... & Alalfy, M. (2019). Serum fetuin A level: a new possible marker for polycystic ovarian syndrome in women with infertility. *Obstetrics and Gynecology Research*, 2(4), 100-107.
10. Escobar-Morreale, H. F. (2018). Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. *Nature Reviews Endocrinology*, 14(5), 270-284.
11. Frhan, B. A. (2003). The effect of IVF Therapy on follicular fluid hormones in female with luteal phase Defect. Thesis, MCS. Collage. Med. University. Baghdad.
12. HAISENLEDER, D. J., DALKIN, A. C., ORTOLANO, G. A., MARSHALL, J. C., & SHUPNIK, M. A. (1991). A pulsatile gonadotropin-releasing hormone stimulus is required to increase transcription of the gonadotropin subunit genes: evidence for differential regulation of transcription by pulse frequency in vivo. *Endocrinology*, 128(1), 509-517.
13. Herman, JP.; Prewitt, CM. and Cullinan. (1996). Neuronal circuit regulation of the hypothalamo, pituitary, adrenocortical stress axis. *Crit.Rev.Neurobiol.*, 10:371-394.
14. Hillier, S. G. (1993). Ovarian stimulation with recombinant gonadotrophins : LH as adjunct to FSH. In: Jacobs, H. S., ed. *The new frontier in ovulation induction* Carnforth, UK: Pathenon: 39-47.
15. Holick H. L. *Biochemistry and physiology-Aspect of Nutrition*. 4th Ed. Mosbey 2004.

16. Ibrahim, Z. M., Kishk, E. A., Fahmy, S. M., & Taha, O. T. (2020). Serum 1, 25-dihydroxy vitamin D-vitamin D₃-among obese Egyptian women with polycystic ovary syndrome. *ObstetGynecol*, 4, 1-3.
17. Jäpelt, R.B and Jakobsen, J. Vitamin D in plants: a review of occurrence, analysis, and biosynthesis. *Front. Plant Sci.* 2013;4(136):1-20.
18. Jhon, G.R. competitive protein binding radio assay for 25(OH) D₃. *J.Clin. Endocr.Metab.*1971;33:992-5.
19. Li, Y., Wang, J., Yang, J., Chen, J., Zhou, W., Qiao, C., ... & Bi, Y. (2021). The correlation between vitamin D, glucose homeostasis and androgen level among polycystic ovary syndrome patients: A cross-sectional study. *Gynecological Endocrinology*, 37(3), 235-239.
20. Liu, S., Hu, W., He, Y., Li, L., Liu, H., Gao, L., ... & Liao, X. (2019). Serum Fetuin-A levels were increased and associated with insulin resistance in women with polycystic ovary syndrome.
21. Mahdi, H. A., & Al-Samarrai, R. R. H. (2021). Evaluation the correlation between the level of asprosin and some biochemical parameters in women with polycystic ovary syndrome. *Samarra Journal of Pure and Applied Science*, 3(2), 12-24.
22. Nelson, V.L.; Legro, R.S.; Strauss, JF III. and McAllister, J.M.(1999). Augmented Androgen Production Is a Stable Steroidogenic Phenotype of Propagated Theca Cells from Polycystic Ovaries. *Mol Endocrinol.*, 13:946-957.
23. Nettore, I.C.; Albano, L.; Ungaro, P.; Colao, A. and Macchia, P.E.Sunshine vitamin and thyroid. *Reviews in Endocrine and Metabolic Disorders.* 2017;18(3):347-54
24. Nowson, C.A. and Margerison, C. Vitamin D intake and vitamin D status of Australians. *Medical Journal of Australia.* 2002;177(3):149-52.
25. Overes, H. W.; de Leeuw, R. and Kloosterboer, H. J. (1992). Regulation of aromatase activity in FSH-primed rat granulosa cells in vitro by follicle stimulating hormone and various amounts of human chorionic gonadotropin. *Hum. Rrprod.*, 7: 191-6
26. Paschou, S.A.; Anagnostis, P.; Karras, S. et al. Bone mineral density in men and children with haemophilia A and B: a systematic review and meta-analysis. *Osteo Inter.* 2014;25(10):2399-407
27. Patel, K., Coffler, M. S., Dahan, M. H., Malcom, P. J., Deutsch, R., & Chang, R. J. (2004). Relationship of GnRH-stimulated LH release to episodic LH secretion and baseline endocrine-metabolic measures in women with polycystic ovary syndrome. *Clinical endocrinology*, 60(1), 67-74.
28. Rachid, S.K.; O Rasheed, B.; M Jaff, P. and A Faraj, K. Vitamin D Status Among Women Living in Sulaimani, Kurdistan Region and HPLC-MS Analysis for Measuring Vitamin D in Organic and Non-organic Eggs. *Kirkuk University Journal-Scientific Studies.* 2017;12.2.
29. Sak, S., Uyanikoglu, H., Incebiyik, A., Incebiyik, H., Hilali, N. G., Sabuncu, T., & Sak, E. (2018). Associations of serum fetuin-A and oxidative stress parameters with polycystic ovary syndrome. *Clinical and Experimental Reproductive Medicine*, 45(3), 116.
30. Stener-Victorin, E., Padmanabhan, V., Walters, K. A., Campbell, R. E., Benrick, A., Giacobini, P., ... & Abbott, D. H. (2020). Animal models to understand the etiology and pathophysiology of polycystic ovary syndrome. *Endocrine reviews*, 41(4), bnaa010.

31. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Get vaccinated when it is your turn and follow the local guidelines. *International Journal of Health Sciences*, 5(3), x-xv. <https://doi.org/10.53730/ijhs.v5n3.2938>
32. Turgeon, GL.; Kimura, Y.; Warimg, DW. And Mellon, PL.(1996). Steroid and pulsatile gonadotropin releasing hormone (GnRH) regulation of Luteinizing hormone and GnRH receptor on a novel gonadotrope cell line. *Mol. Endocrinol.*, 10:439-45.
33. Ubaid, M. M., & Rahma, J. H. (2022). The effect of sex hormones on progression of *Leishmania donovani* infection in liver and spleen of BALB/c mice. *International Journal of Health Sciences*, 6(S3), 6327–6337. <https://doi.org/10.53730/ijhs.v6nS3.7404>
34. Vale, W.; Waiter, E.; Gray, P.; Harrison, C.; Bilezikjian, L. and Choe, S. Actives and Inhibins and their signaling. *Annals of the New York Academy of Sciences*. (2004); 1038:142-7
35. Wolf, W. M., Wattick, R. A., Kinkade, O. N., & Olfert, M. D. (2018). Geographical prevalence of polycystic ovary syndrome as determined by region and race/ethnicity. *International journal of environmental research and public health*, 15(11), 2589.