IJIMM, Volume 2, Issue 8, 2024 ISSN: 2995-5319
http://medicaljournals.eu/index.php/IJIMM/issue/view/3

INTERNATIONAL JOURNAL OF INTEGRATIVE AND MODERN MEDICINE

Study of the Therapeutic Effect of Some Hormonal Disorders Associated With Polycystic Ovary Syndrome in Iraqi Women

Zahraa Hatem Abdulla, Evan Mohammad Mustafa, Sahla Khurshid Abbass
College of Science, Kirkuk University, Iraq

Annotation: Background: Polycystic ovary syndrome (PCOS) is a hormonal imbalance resulting from high levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) in females, leading to immaturity of eggs, ovarian cysts, irregular menstrual cycle, infertility, excessive facial hair growth, and acne. **Materials and Methods:** This study was conducted to follow up the therapeutic effect on some blood and hormonal variables of 35 patients with polycystic ovary syndrome (PCOS) from women suffering from infertility and infertility, and who visited Azadi Teaching Hospital and private laboratories in Kirkuk city, their ages ranged between (18 - 40 years). Sample collection and follow-up began by observing some clinical signs in addition to verifying the results of ultrasound examinations from early February 2023 to early November 2023. Each patient's examinations were followed up before treatment and three months after taking the treatment. **Result:** The results we obtained after three months of treatment were compared with the results of the examinations of the patients in the pre-treatment stage and the control group. The treatment plan was based on modifying the patient's dietary lifestyle by following a healthy diet and giving treatment represented by oral contraceptives, fertility drugs and the use of sugar-lowering drugs such as Glucophage or Metformin, in addition to nutritional supplements such as antioxidants. **Conclusion:** The results showed a significant decrease in the level of hemoglobin before and after treatment compared to the control group. Other blood variables did not show any significant differences ($0.05 < p$). Pituitary hormones (LH, FSH) showed a significant decrease at a significant level ($0.000 > p$) respectively after three months of continuing to take the treatment. They also showed the therapeutic effect of improving the level of thyroid-stimulating hormone TSH and T3 changed numerically and not significantly after (3) months of taking the treatment compared to the pre-treatment stage and the control group. As for the T4 hormone, it did not show any significant differences during the treatment period. The therapeutic effect on the leptin hormone showed a significant decrease at a level ($0.001 > p$).) After three months of taking the treatment compared to the pre-treatment stage and the control group.

1.1 Introduction

Polycystic ovary syndrome (PCOS) is a reproductive disorder of ovarian function in some women, associated with high levels of androgens, hyperinsulinemia, and chronic anovulation (1), but the cause is still unclear, as the endocrine system, reproductive system, and metabolism are affected by this syndrome and it is a major cause of infertility in women (2). One in every (5-6) women faces serious complications related to infertility and irregular menstrual cycles (3). This endocrine disorder affects women under the age of (18_44) years and affects (5-15%) of women worldwide (4).

The normal function of hormones plays an important role in regulating ovarian function and the menstrual cycle, thus maintaining fertility. If female hormone levels remain unbalanced, this may lead to impaired ovarian function, leading to the formation of cysts within the ovaries. Although the main cause of this syndrome is unknown, several factors have been identified that affect it, such as genetic factors, environmental factors, insulin resistance, stress, and increased androgen production, and Metabolic disorders (6,5). The syndrome leads to disturbances in fat distribution and cardiovascular diseases, which are one of the main causes of death worldwide (7). Heart diseases represent a group of disorders that affect the heart and blood vessels (8). There are many factors that affect a woman's ability to reproduce (9), including age, smoking, stress, excessive alcohol consumption, malnutrition,

sexually transmitted diseases (6,5), and medical disorders associated with infertility in women, which also play a role in the development of sexual dysfunction (10), such as polycystic ovary syndrome (PCOS), which is the most common cause of ovulation failure in infertile women (3), as well as premature ovarian failure, uterine fibroids (11), hypothalamic insufficiency, hyperprolactinemia, and hormonal disorders (12).

Follicle stimulating hormone is the main hormone in the follicular phase, where it stimulates the formation and growth of eggs (vale), while luteinizing hormone is the main hormone in the luteal phase and stimulates the ovulation process. Any imbalance in the levels of FSH and LH hormones may lead to disorders in the reproductive function of the ovary, including: menstrual cycle disorders, delayed childbearing or infertility (13).

Thyroid hormones play an important role in the processes of growth, differentiation, metabolism and reproduction. The secretion of these hormones is regulated by thyroid stimulating hormone (TSH), which is secreted by the pituitary gland from the anterior lobe (14).

Leptin is a protein hormone produced and secreted by white adipose tissue. Increasing the amount of adipose tissue leads to an increase in the concentration of leptin, which leads to a reduction in energy consumption, as it plays an important role in energy balance and regulating its consumption (15).

1.2 Aims of the study

Follow up the therapeutic effect followed for patients on some blood parameters including hemoglobin level Hb and measurement of total white blood cell count WBC and platelets PLT after three months of taking the treatment compared to the pre-treatment stage and the control group, follow up the therapeutic effect followed for patients on some blood parameters including hemoglobin level Hb and measurement of total white blood cell count WBC and platelets PLT after three months of taking the treatment compared to the pre-treatment stage and the control group.

2. Materials and Methods

2.1 Study site and sample collection:

The study samples were collected from the patients who visited the gynecological consultant and the infertility center at Azadi Teaching Hospital in Kirkuk after diagnosing their condition with ultrasound and diagnosing the clinical signs of the syndrome in them, including menstrual disorders, infertility, hirsutism, weight gain and acne, according to a special questionnaire prepared for this purpose. The condition of each patient was followed up 3 months after treatment, and patients who had been treated previously were excluded. The ages of the patients ranged between (18_40) years. The period of sample collection and follow-up took less than a year from (early February 2023 to November 2023). In addition to the patients' samples, blood samples were collected from healthy women who did not suffer from the above disorders, amounting to (20) blood samples, and each sample was subjected to a set of tests required to be followed up, which are blood and hormonal variables.

2.2 Collection of blood samples

Blood samples of 5 ml of venous blood were drawn after confirming that they had polycystic ovary syndrome during the follicular phase of the menstrual cycle in the morning. After that, 2 ml of blood were placed in a tube containing the anticoagulant EDTA for the purpose of measuring the total and differential count of white blood cells and measuring the percentage of hemoglobin in the blood, while 3 ml of blood were separated into a special Gel Tube and left for a period of 10-15 minutes at room temperature, then centrifuged at a rate of 4000 rpm for 15 minutes to separate the blood serum, which represents the upper filtrate, using a micro pipette. After that, the serum was distributed into small Eppendorf tubes and several replicates were kept for each sample to prevent repeated thawing. Then the samples were kept at a temperature of 20 Celsius for the purpose of conducting other serological and hormonal tests.

2.3 Hematological Tests

The total number of white blood cells (WBC), platelets (platelt) and hemoglobin (Hb) was calculated using an Auto analyzer hematology device called swelab, which is a Swedish device. This device depends on the cellular count of different types of blood cells automatically through the scanner mechanism in it. The sizes and diameters of the cells differ, which leads to a difference in their ability to pass light. A capillary tube is placed inside the EDTA Tube, and by pressing the start button, the device begins to withdraw 10 microliters of blood after about one minute, the device shows the results on the screen.

The concentration of hormonal variables in the blood serum of all women with polycystic ovary syndrome and healthy women was measured by following the steps accompanying the ready-made kit imported from the American company (USCN) for the Cobas c601 device.

The concentration of leptin hormone was measured in the blood serum of all women with polycystic ovary syndrome Multi-step by following the steps attached with the ready-made kit imported from the American company (USCN) and the special Elisa.

3. Results and discussions

Hematological variables studied for the control group and the patient group before and after treatment. The results of the current study recorded a significant decrease (p>0.000) in the blood hemoglobin level in women with PCOS syndrome before treatment (0.18±11.09)) and after treatment for 3 months (0.15±11.74) compared to the control group (0.23±12.66). The results of the current study recorded a numerical, but not significant, increase in the level of white blood cells in women with PCOS syndrome, before treatment (0.51±7.16) and after treatment for 3 months (0.33±7.72) compared to the control group (0.29±6.67). As for platelet cells, a numerical change was recorded in women with PCOS before treatment (231.485±12.946) and after 3 months of treatment (13.05±230.45) compared to the control group (14.86±252.65). The current study also showed statistically significant differences in the various blood values between women with PCOS before treatment and after 3 months of treatment compared to the control group, while the study showed no significant differences in the levels of the total number of white blood cells and the number of platelets. Hormonal levels in women with PCOS affect hemoglobin levels, and testosterone stimulates the production of white blood cells, and therefore androgen affects bone marrow cells through androgen receptors in the bone marrow. It is believed that the decreased menstrual frequency in women with PCOS causes differences in hemoglobin levels between women without PCOS and that the therapeutic effect led to a significant decrease in the level of Hb, WBC white blood cell and platelet cells after three months of taking the patients' treatment compared to the pre-treatment stage and the control group. As shown in the table, improving insulin sensitivity contributes to reducing the level of white blood cells (WBC). The study conducted by (16) also showed that metformin reduces the total white blood cell (WBC) count resulting from inflammation in the case of PCOS after a period of treatment that lasts for 3 months, which helps prevent chronic inflammation.

Table (1): shows some blood variables of the study samples before and after treatment and the control group for three months:

Variables studied	Control group	Before treatment	Before treatment	*P*_ Value
Mean ± St. Error				
Hb g/dL	a 12.66±0.23	c 11.09±0.18	b 11.74±0.15	0.000
WBC ($\times 10^3$cell/mm^3)	a 6.67±0.29	a 7.16±0.51	a 7.72±0.33	0.26

PLT ($\times 10^3$cell/mm^3)	a 252.65±14.86	a 231.48±12.94	a 230.45±13.05	0.52

Effect of hormonal factors in women with PCOS

The results of the current study recorded a significant increase (p>0.000) in the level of luteinizing hormone (LH) in women with PCOS before treatment (18.18±0.47 mlu/ml) and after treatment (11.66±0.32 mlu/ml) compared to the control group (7.01±0.29 mlu/ml). This is consistent with (17,18) In Karbala, high levels of LH are an important feature of polycystic ovary syndrome (20,19). LH receptors are expressed in theca cells, corpus luteum cells, granulosa cells, and uterus. It is necessary to stimulate follicle growth, oocyte maturation, and ovulation (21,22). High levels of LH lead to a defect in the ovulation process in the follicular cycle, and high levels of it inhibit the activity of aromatase and inhibit the growth of the oocyte (23) On the other hand, the majority of women with polycystic ovary syndrome suffer from increased insulin or insulin resistance, as well as obesity, which in turn leads to a malfunction in the ovarian-pituitary-hypothalamic axis. Insulin increases the pulse of the releasing hormone GnRH, which leads to an increase in the luteinizing hormone LH. As for the follicle-stimulating hormone (FSH), it recorded a significant increase (p>0.000) in women with polycystic ovary syndrome before treatment (7.98±0.25 mlu/ml) and after treatment (6.86±0.19 mlu/ml) compared to the control group (5.99±0.24 mlu/ml). This is consistent with (16), where they mentioned a significant increase in the pre-treatment phase. FSH (follicle-stimulating hormone) is the main hormone in the follicular phase of the menstrual cycle, as it works to activate the formation and maturation of eggs (ova) and thus the secretion of estrogen from the mature egg (24). In contrast, LH (luteinizing hormone) is the main hormone in the luteal phase of the menstrual cycle, as it stimulates ovulation and the formation of progesterone in the corpus luteum phase. Any imbalance in the levels of LH and FSH hormones is reflected in the levels of progesterone and estrogen hormones in addition to testosterone, which leads to disorders in the reproductive functions of the ovary. The presence of any imbalance in the pituitary-hypothalamic axis leads to increased pulsatile release of LH hormone from the hypothalamus, which raises the ratio of LH hormone to FSH hormone to more than 2.5. As a result, ovulation does not occur and cysts form in the ovary, which causes a delay in menstruation or a delay in pregnancy (25). This is inconsistent with (27,26).

Table (2): shows the concentration of follicle-stimulating hormone and luteinizing hormone in the study samples:

Hormonal factors	**Control group**	**Before treatment**	**After treatment**	***P*_ Value**
Mean ± St. Error				
LH (mlu/ml)	c 7.01± 0.29	a 18.18±0.47	b 11.66±0.32	0.000
FSH (mlu/ml)	c 5.99 ±0.24	a 7.98±0.25	b 6.86± 0.19	0.000

Effect of thyroid hormones

As for the results of thyroid hormones, it was found that the thyroid stimulating hormone TSH showed a numerical but not significant change in women with PCOS before treatment (mu/L 0.29±2.24) and after 3 months of treatment it was (mu/L 0.26±1.97)) compared to the control group (mu/L 0.21±2.20). As for the T3 hormone shown in Table (3), a significant difference appeared for the T3 hormone in women suffering from polycystic ovary syndrome, before treatment (1.52±0.13 ng/ml) and after 3 months of treatment (ng/ml 1.57±0.12) compared to the control group (1.10±0.05 ng/mI). As for the T4 hormone level shown in Table (3), it did not show a significant difference in women with polycystic ovary syndrome, before treatment (9.62±0.44 Mg/dl) and after 3 months of treatment (Mg/dl 9.68±0.38) compared to the control group (Mg/dl 8.80±0.19). This is consistent with (28) and

not consistent with (29) who found that thyroid disorders were detected in 16% of women with polycystic ovary syndrome. Moreover, this study revealed that there were no statistically significant differences in the levels of TSH, T3 and T4 in all the studied factors in both the thyroid gland and the ovaries. Recent studies have shown many evidences that women suffering from polycystic ovary syndrome show thyroid disorders in most cases, especially those suffering from hypothyroidism or at risk of hypothyroidism in the future (30). Hypothyroidism may lead to low levels of sex hormone-binding globulin (SHBG), which in turn leads to high levels of testosterone, one of the factors that contribute to the appearance of some symptoms of PCOS syndrome such as hirsutism, acne, and infertility (31). The statistical results of the studied samples, as shown in Table (3), showed that the TSH hormone showed a significant decrease compared to the pre-treatment stage after 3 months of taking thyroxine hormone treatment at doses ranging between (100_50) mg/day according to what the patients need, accompanied by continued taking metformin treatment. This significant decrease in TSH improved the levels of thyroid hormones T4 and T3 in the studied sample.

Table (3): shows the concentration of thyroid hormones in the study samples:

Hormonal factors	Control group	Before treatment	After treatment	*P*_ Value
Mean ± St. Error				
TSH mu/L	2.20±0.21	1.97±0.26	2.24±0.29	0.74
T3 ng/ml	b 1.10±0.05	a 1.52±0.13	a 1.57±0.12	0.04
mg/dl T4	a 8.80±0.19	a 9.62±0.44	a 9.68±0.38	0.31

Leptin hormone in women with PCOS syndrome

The results shown in Table (4) showed a significant increase (0.001> p) in the level of leptin hormone in the group of patients before treatment and after treatment, reaching (7.33±339.37 pg/ml) (12.28±186.66 pg/ml) respectively compared to the control group (3.27±110.48 pg) ml). The results of the current study agreed with studies (33,32), and that the increase in the level of the hormone may be due to its production from pre-ovulatory follicles that express the leptin gene in granulose cells (34), and that the increasing numbers of these follicles in the case of polycystic ovary syndrome led to excessive production of leptin and thus to an increase in its level in polycystic ovary syndrome patients (35). High levels of leptin can cause leptin resistance, which impedes follicle maturation through leptin inactivation in theca cells, thus reducing the blood vessels that leptin participates in forming around the follicle, leading to hypoxia within the follicles and negatively affecting their maturation, thus impeding the ovulation process (36). High levels of insulin and insulin resistance, which are characteristic of obese women with polycystic ovary syndrome, can also cause high levels of leptin (37,38). The results of the current study showed a significant decrease after 3 months of taking the treatment compared to the pre-treatment stage and the control group, as shown in Table (4). Our results agreed with a study conducted by (16), which indicated the role of metformin treatment in reducing leptin resistance in PCOS patients, which in turn improved and regulated the level of ovulation in PCOS patients.

Table (4): shows the levels of leptin hormone in samples of women with polycystic ovary syndrome before and after treatment:

Immune factor	Control group	Before treatment	After treatment	*P_Value*
Mean ± St. Error				
Leptin (pg/ml)	c 110.48± 3.27	a 339.37± 7.332	b 186.66±12.	0.001

4. Conclusions

The study achieved through the treatment followed by taking birth control pills and metformin continuously for 3 months and regularly improving the levels of pituitary hormones (LH, FSH) and regularizing the menstrual cycle, the therapeutic effect had a major role in reducing the levels of the thyroid hormone T3 as well as reducing the leptin hormone.

5. Recommendations

Study the syndrome in unmarried women, especially those aged between (16-25) years, and prepare educational and research plans in high schools and universities about this syndrome to reduce the risks of neglecting it, researchers urged to study PCOS during pregnancy because of the impact of this syndrome on the health of the fetus and the occurrence of recurrent miscarriages, a study on the specific genes responsible for polycystic ovary syndrome,a molecular study on reproductive hormone receptors and their relationship to the syndrome, a study on large samples and follow-up treatment for periods of more than three months and their relationship to hormonal indicators and conduct studies on the Anti-Mullerian Hormone hormone and its relationship to PCO.

Acknowledgment

We would like to acknowledge the University of Kirkuk/College of Science/ Department of Biology for the support and the Azadi hospital/Kirkuk for help and scientific advices,I would like to extend my thanks and gratitude to the staff of the Azadi Teaching Hospital Laboratory in Kirkuk Governorate/Iraq and the laboratory staff. I would also like to extend my gratitude to everyone from (Infertility Department, Gynecology Consultation Department) at Azadi Teaching Hospital. May Allah reward you with the best reward. I would also like to thank Dr. Jassim Muhammad Fayyadh, who helped me in the statistical analysis, and my sincere thanks to the staff of the Middle East Laboratory for their assistance.

References

1. Dubey, P., Reddy, S., Boyd, S ,.Bracamontes, C., Sanchez, S., Chattopadhyay, M & ,.Dwivedi, A. (2021). Effect of Nutritional Supplementation on Oxidative Stress and Hormonal and Lipid Profiles in PCOS-Affected.
2. Eiras MC, Pinheiro DP, Romcy KAM, Ferriani RA, Dos Reis RM, Furtado CLM.(2021). Polycystic Ovary Syndrome: the Epigenetics Behind the Disease. Reprod Sci: 1-15. Dunaif A. Polycystic ovary syndrome in 2011: Genes, aging and sleep apnea in polycystic ovary syndrome. Nature reviews Endocrinology. 8(2): 72.
3. Kathleen M Hoeger, Anuja Dokras, Terhi Piltonen.(2021) Update on PCOS: Consequences, Challenges, and Guiding Treatment, The Journal of Clinical Endocrinology & Metabolism, Volume 106, Issue 3, March 2021, Pages e1071-e1083
4. Azziz, R. (2016). Introduction: Determinants of polycystic ovary syndrome .Fertility and Sterility, 106(1), 4-5.
5. Kasililika, A. G., Odukogbe, A. T. A., Dairo, M. D., Balandya, B. S., & Bunuma, E. K. (2021). Lifestyle and oxidative stress status in infertile women in Dar es Salaam, Tanzania: comparative cross-sectional study. Middle East Fertility Society Journal, 26(1), 1-8.
6. Rooney, K. L., & Domar, A. D. (2022). The relationship between stress and infertility. Dialogues in clinical neuroscience. 143(2), 85-88
7. Yusuf,S.,Reddy,S., Ounpuu,S.Anand,S.Global burden of cardiovascular diseases : part I : general considerations ,the epidemiologic transition , risk factors ,and impact of urbanization. Circulation .2001 ;104(22):2746.
8. Alnajjar,M.K.,Abu-Naser ,S.S.Heart sounds analysis and classification for cardiovascular diseases diagnosis using deep learning ,Int.J.Aca.Eng.Res.2022;6(1):7-23.

9. Somigliana, E., Paffoni, A., Busnelli, A., Filippi, F., Pagliardini, L., Vigano, P., & Vercellini, P. (2016). Age-related infertility and unexplained infertility: an intricate clinical dilemma. Human Reproduction, 31(7), 1390-1396.
10. Practice Committee of the American Society for Reproductive Medicine. (2021). Fertility evaluation of infertile women: a committee opinion. Fertility and Sterility, 116(5), 1255-1265.
11. Altaee HA; Almadfa ZA; Alkhafaji ZH.(2013). Effect of obesity on ovarian reserve parameters in mid-reproductive agewomen, F1000Research 1:43
12. Chen, J., & Katznelson, L. (2022). The role of growth hormone for fertility in women with hypopituitarism. Growth Hormone & IGF Research ,pp: 63, 101458.
13. Carson, S. A., & Kallen, A. N. (2021). Diagnosis and management of infertility: a review. Jama, 326(1), 65-76.? ISO 690.
14. Shams Al-Din, Nouri Nouri Bashboush and Habib, Sanaa Obaidi. (2014). Study of reproductive hormonal changes in polycystic ovary syndrome in women affected by reproductive age in Najaf city, Journal of University of Kufa Life Sciences; 6 (3): 7-1.
15. Silva JF, Ocarino NM, Serakides R. (2018).Thyroid hormones and female reproduction. Biol Reprod Nov 1;99(5):907-921. doi :10.1093 /biolre/ioy115. PMID :29767691.
16. Childs,G.V.,Odle,A.K.,MacNicol,M.C.,& MacNicol ,A.M. (2021) .The importance of leptin to reproduction .Endocrinology ,162(2) ,bqaa204.
17. Youssef, Mai Nafeh and Ahmed, Munif Saab (2017) Study and follow-up of the therapeutic effect of some hormonal disorders associated with polycystic ovary syndrome in women in Tikrit city, Journal of the City of Science University College. 9.2. pp. 125-129.
18. Jadav, P. M. (2020). A study of Follicle Stimulating Hormone (FSH) and Luteinizing Hormone (LH) in women of Polycystic Ovarian Disease (PCOD) at Tertiary Care Hospital of Gujarat, India. International Journal of Clinical Biochemistry and Research, 5(1), 112–115. https://doi.org/10.18231/2394-6377.2018.0022
19. Al-Mayahy, Laheeb Shaker Mahmoud (2021): Association of zinc alpha 2 glycoprotein and heat shock protein 70 with polycystic ovary syndrome in infertile Iraqi women. Master's thesis, College of Medicine, University of Karbala.
20. Zhang, Y.; Meng, F.; Sun, X.; Sun, X.; Hu, M.; Cui, P. and Wu, X.-K.(2019). Hyperandrogenism and insulin resistance contribute to hepatic steatosis and inflammation in female rat liver. Oncotarget , 9, 18180–18197.
21. Baldani, D. P.; Skrgatic, L.; Kasum, M.; Oguic S. K. and Herman M. (2019). Altered leptin, adiponectin, resistin and ghrelin secretion may represent an intrinsic polycystic ovary syndrome abnormality,Gynecological Endocrinology,35:5, 401-405.
22. Deswal, R.; Nanda, S. and Dang, A. S. (2019). Association of Luteinizing hormone and LH receptor gene polymorphism with susceptibility of Polycystic ovary syndrome. Systems biology in reproductive medicine, 65(5), 400-408.
23. Choi, J. and Smitz, J. (2014).Luteinizing hormone and human chorionic gonadotropin: distinguishing unique physiologic roles. Gynecol Endocrinol 30, 174–181.
24. Al-Jubouri, Liqa Hassoun Sakban (2014). Molecular and physiological study of polycystic ovary syndrome in women in Karbala Governorate - University of Karbala, College of Education for Pure Sciences - PhD thesis
25. Vale W, Wiater E, Gray P, Harrison C, Bilezikjian L, Choe S. (2004) Activins and inhibins and their signaling. Ann N Y Acad Sci. Dec ;1038:142-7.doi: 10.1196/annals.1315.023.PMID : 15838109.

26. Banaszewska B, Spaczyński RZ, Pelesz M, Pawelczyk L. (2003). Incidence of elevated LH/FSH ratio in polycystic ovary syndrome womenwith normo- and hyperinsulinemia. Annals Academiae. Medicae Bialostocensis. 48: 132-134.

27. Ran, Y.; Yi, Q. and Li, C. (2021). The Relationship of Anti-Mullerian Hormone in Polycystic Ovary Syndrome Patients with Different Subgroups. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 14, 1419.

28. Esmaeilinezhad, Z.; Babajafari, S.; Sohrabi, Z.; Eskandari, M. H.; Amooee, S. and Barati-Boldaji, R. (2019). Effect of synbiotic pomegranate juice on glycemic, sex hormone profile and anthropometric indices in PCOS: A randomized, triple blind, controlled trial. Nutrition, Metabolism and Cardiovascular Diseases, 29(2), 201-208.

29. AlFaisal, A. H. M. and Al-Deresawi, M. S. G. (2013). The correlation between thyroid hormones, reproductive hormones, body mass index (BMI) and hirsute in Iraqi women with polycystic ovary syndrome (PCOS). J of Univ. Anbar Pure Science, 7: 1-6.

30. Zwain, Z.M. and Aziz M. K. (2016). Polycystic ovarian syndrome and thyroid disorders. J. of Technical Research and Applications, 4(5):73-77.

31. Allahbadia,G.N .and Merchant, R.(2011). Polycystic ovary syndrome and impact on health. Middle East Fertity Society, 16:19–37.

32. Dittrich, R.; Kajaia, N.; Cupisti, S.; Hoffmann, I.; Beckmann, M. W. and Mueller, A. (2009). Association of thyroid-stimulating hormone with insulin resistance and androgen parameters in women with PCOS. Reproductive Biomedicine Online, 19(3): 319-325.

33. Kargasheh, F. B.; Ansaripour, S.; Borumandnia, N.; Moradi, N.; Zandieh, Z.;Maleki, M. and Vatannejad, A. (2021). Association of leptin G2548A and leptin receptor Q223R polymorphisms and their serum levels with infertility and recurrent pregnancy loss in Iranian women with PCOS. Plos one, 16(8), e0255920.

34. Salem A. M. (2021). Variation of Leptin During Menstrual Cycle and Its Relation to the Hypothalamic-Pituitary-Gonadal (HPG) Axis: A Systematic Review. International journal of women's health, 13, 445–458.

35. Yonis, R. A.; Fadhila S. Al-Doski.(2020). "Fluctuation of Serum Leptin Through Menstrual Cycle in Young Fertile Women in Mosul City". Annals of the College of Medicine, Mosul, 41, 2, 125-131.

36. Anwar, A. A.; Abdullah, N.; Padjalangi, A. N.; Hamid, F.; Mappeware, N. A. andLukas, E. (2021). Serum leptin concentration is correlated to insulin resistance in polycystic ovary syndrome (PCOS) patients. Molecular and Cellular Biomedical Sciences, 5(2), 93-7.

37. Namavar Jahromi, B.; Dabaghmanesh, M. H.; Parsanezhad, M. E. and Fatehpoor, F. (2017). Association of leptin and insulin resistance in PCOS: A case-controlled study. International journal of reproductive biomedicine, 15(7), 423–428.

38. Rashid, A.; Ganie, M. A.; Wani, I. A.; Bhat, G. A.; Shaheen, F.; Wani, I. A. and Shah, Z. A. (2020). Differential impact of insulin sensitizers vs. anti-androgen on serum leptin levels in Vitamin D replete PCOS women: a six month open labeled randomized study. Hormone and Metabolic Research, 52(02), 89-94.