International Journal of Health Systems and Medical Sciences
ISSN: 2833-7433
Volume 03 Number 03 (2024)
Impact Factor: 10.87
SJIF (2023): 3.656

www.inter-publishing.com

Article

Relationship Of Thyroid Hormones, Prolactin, Leptin Level, And Some Physiological And Biochemical Parameters In Affected Women Polycystic Ovary Syndrome In Samarra City And Its Surrounding Areas

Khalida Khaleel Abdullah[1], Asmaa Ismael Hussein[2]

1,2 Department of Biology, College of Education, University of Samarra, Salah Al-din, Iraq
* Correspondence: Khaleda.kh@uosamarra.edu.iq

Abstract: This study aimed to analyze the levels of hormones such as TSH, T3, T4, Prolactin, Leptin, LH, and FSH, as well as to assess the levels of specific antioxidants (GSH, CAT, SOD) and oxidative stress marker (MDA) in married women with polycystic ovary syndrome (PCOS) in Samarra and nearby regions. The results revealed a significant increase (P≤0.05) in the levels of Prolactin, Leptin, FSH, LH, TSH, T3, and T4, along with a rise in BMI and MDA, which indicates oxidative stress. Conversely, a significant reduction (P≤0.05) in antioxidant levels (GSH, CAT, SOD) was observed in the patients compared to the control group.

Keywords: Polycystic Ovaries Syndrome (PCOS), Follicular Stimulating Hormone(FSH), Luteinizing Hormone (LH), Prolactin, Leptin

1. Introduction

Polycystic ovaries syndrome is one of the most common cases of hormonal imbalance in women, but the exact mechanism of polycystic ovary syndrome is not known. Therefore, the main cause is unknown, but there are several factors that lead to it, including the autosomal dominant genetic factor. Heredity is one of these factors. A woman who has one or more individuals in her family. Someone with this syndrome (such as a mother or sister) is more susceptible to it than anyone else In addition to another factor, it is the insulin hormone, as it was found that most women who suffer from PCOS have high insulin, which is in the form of insulin resistances and causes an increase in Testosterone hormone secreted from the ovaries, which in turn causes excessive obesity, the appearance of acne, and coarse hair, which are called hormonal disorders [1].

Polycystic ovary syndrome (PCOS) is a prevalent and multifaceted endocrine condition, affecting between 5-20% of women of reproductive age [2], with both immediate and long-term impacts [3]. It is one of the primary causes of ovulatory dysfunction, affecting 3-13% of women. Women diagnosed with PCOS experience a range of metabolic, endocrine, and psychological issues, and are at an elevated risk for pregnancy complications, such as gestational diabetes and preterm delivery [4].

A disturbance in the hypothalamic-pituitary axis leads, as a result, to a defect in the hormonal system of the reproductive system, so the production of female hormones such as estrogen and progesterone decreases, and the production of male hormones increases, hyperandrogenism, which causes hirsutism and acne. Also, a disturbance in the

Citation:. Khalida Khaleel Abdullah. Relationship Of Thyroid Hormones, Prolactin, Leptin Level, And Some Physiological And Biochemical Parameters In Affected Women Polycystic Ovary Syndrome In Samarra City And Its Surrounding Areas International Journal of Health Systems and Medical Sciences 2024, 3(3), 277-285.

Received: 10th Apr 2024
Revised: 11th Mei 2024
Accepted: 24th Jun 2024
Published: 27th Jul 2024

production of female hormones leads to The growth of some ovarian follicles and the accumulation of fluids inside them, forming a state of cysts and thus non-ovulation. Also, a disturbance in the production of female hormones leads to the growth of some ovarian follicles and the accumulation of fluids inside them, forming a state of cysts and thus non-ovulation .Insulin resistance In female patients, it is more apparent in women with chronic anovulation than in women who have normal, periodic ovulation. This condition is diagnosed in 50% of women with anovulation, as shown by Kauffman and his group [5].

Polycystic ovary syndrome (PCOS) impacts various aspects of health and quality of life throughout a woman's lifespan, owing to its effects on reproduction, metabolism, and mental well-being. It is a leading cause of ovulatory disorders and is closely linked to obesity, type 2 diabetes, metabolic syndrome, and cardiovascular risk factors such as high blood pressure, eating disorders, and anxiety. and depression[6].

2. Materials and Methods

Collection of blood samples

The study samples were gathered from health centers and private laboratories in Samarra and its surrounding regions. A total of 60 women, aged between 20 and 40, participated in the study. These participants were divided into two groups: the first group comprised 40 married women diagnosed with polycystic ovary syndrome (PCOS), while the second group included 20 married, non-pregnant women who did not use contraceptives and served as the control group.

A 10 ml blood sample was collected from women with PCOS on the second or third day of their menstrual cycle to assess various hormones, including FSH, LH, PRL, TSH, T3, T4, and leptin. Additionally, several biochemical tests were performed. The blood was allowed to sit in test tubes for 10 to 15 minutes at room temperature, followed by centrifugation at 3000 rpm for 5 minutes. The serum, which formed the top layer, was then separated using a micropipette. The serum was frozen after being divided into multiple test tubes for further analysis of the specified hormones and biochemical markers.

Method work:

BMI : was calculated by dividing body weight in kilograms by the square of height in meters.

BMI = weight (kg) / height squared (m2) [7]

Leptin, Prolactin: The concentration of the hormone leptin was measured using the ELISA kit manufactured by Assaypro (Petridou et al., 2005), and the concentration of the hormone prolactin was measured by following the steps included with its ready-made analysis kit [8]

TSH, T3, T4: The concentration of TSH was measured using the ELISA kit numbered BC-1003 manufactured by the Spanish company Bio Cheak and T3 and T4 manufactured by Atlas Medica [9].

FSH, LH: LH was measured by adhering to the procedures outlined in the ready-to-use analysis kit [9]. Similarly, FSH levels were determined according to the steps provided in the analysis kit, following the manufacturer's guidelines for the ELISA method [10].

Oxidation balance - antioxidants:

MDA: used the modified thiobarbituric acid (TBA) reaction method used by researchers [11].

CAT: method principle involves the reaction of ammonium metaphenadate with hydrogen peroxide under acidic conditions [12]

Glutathione: Ellmans model and the effectiveness of glutathione concentration in blood serum was estimated using the reagent method [13]

Superoxide dismutase: The activity of the enzyme superoxide dismutase was estimated using the modified photochemical method[13,14]

Statistical analysis:

The statistical program (T.test) was used with a probability concentration of (P≤0.05) [15].

3. Results and Discussion

Table (1) TSH, T3, T4, and BMI levels.

Parameter / Group	TSH (U/l)	T3 (nmo/l)	T4 (nmo/l)	BMI (Kg/m^3)
Patients (infected) N=40	5.98±1.2*	1.37±0.01	88.78±3.05	32.25*
Control N=20	2.31±0.4	1.94±0.04*	125.6±4.08*	28.45

.) There are significant differences when concentration probability (P≤0.05 •
Mean±S.D. Arithmetic mean±standard deviation. •
N = number of samples. •

Table (2) Leptin, PRL, FSH, and LH levels.

Parameter / Group	Leptin (ng/ml)	PRL (ng/ml)	FSH (mlu/ml)	LH (mlu/ml)
Patients (infected) N=40	36.72±2.23*	27.22±1.5*	11.o6±04*	16.9±1.7*
Control N=20	17.38 ±2.03	6.33±0.2	5.98±0.9	7.76±o.9

.) There are significant differences when concentration probability (P≤0.05 •
Mean±S.D. Arithmetic mean±standard deviation. •
N = number of samples. •

Table (3) MDA, GSH, CAT, and SOD levels

Parameter / Group	MDA (µmol/L)	GSH (µmol/L)	CAT (KU/L)	SOD (U\L)
Patients (infected) N=40	9.02±1.9*	0.15±0.01	34.95 ± 0.65	10.28 ± 0.30
Control N=20	4.05±1. 7	0.29±0.04*	58.25 ± 1.09*	15.41± 0.12*

.) There are significant differences when concentration probability(P≤0.05 •
Mean±S.D. Arithmetic mean±standard deviation. •
N = number of samples. •

The study results, as presented in Table (1), indicated a significant rise (P≤0.05) in body mass index (BMI). Weight gain is a common symptom among women with polycystic ovary syndrome (PCOS), and the progression of the condition contributes to this increase [16]. Excessive obesity plays a crucial role in the interrelated functional and reproductive changes, which are key characteristics of PCOS. Suffering from PCOS, increased body mass (BMI) affects metabolism as well as its effect on insulin sensitivity and various steroid hormones in men and women. Rapid changes in body composition and the amount of fat must be monitored through the nutritional program because excessive food intake adds calories to the total. of calories in the body, and this leads to the accumulation of fat and thus leads to an increase in body weight ([17,18]. Controlling the nutritional program is not easy, as the patient needs continuous exercise, especially in the first phase of the program, while long-term programs are more difficult to maintain a normal weight [19].

The study results revealed a significant decrease (P≤0.05) in T3 and T4 hormone levels, along with an increase in TSH hormone levels, in women with polycystic ovary syndrome [20]. Evidence indicates that the normal functions of the reproductive system depend on the effectiveness of thyroid hormones and that any deficiency Or an increase in the secretion of thyroid hormones may lead to a disruption in ovarian function and then stop reproductive cycles, as the natural pattern of reproductive cycles requires a high level of thyroid hormones. It must be noted that reproduction continues in most species after removing the thyroid gland, but productivity is below The normal level. A large number of female patients who suffer from PCOS are accompanied by a state of hypothyroidism due to high levels of the TSH hormone. The thyroid gland and its deficiency is behind causing an increase in the size of the ovary and the formation of cysts inside it, as its deficiency is a contributing factor in Causing cysts [21].

The study also demonstrated a significant rise (P≤0.05) in leptin and prolactin hormone levels, as detailed in Table No. (2). Leptin levels increase with weight gain and obesity and contributes to the development of insulin resistance [22,23]. The total leptin level is associated with metabolic processes, especially with lipid levels [24]. As for the hormone prolactin, it is another reason for the occurrence of menstrual cycle and ovulation disorders because a high elevation of the hormone prevents the binding of FSH to its receptors, FSH receptor, located on the theca cells, which leads to the inhibition of estrogen production [25,26], this may be attributed to an increase in steroids, where negative feedback mechanisms cause elevated prolactin (PRL) levels. Studies have shown that a reduction in estrogen levels and an increase in testosterone and PRL levels are associated with this effect, results in infertility or ovulation disorders. There are also chemicals that affect the hypothalamic dopamine system or Dopamine receptors can increase the concentration of the PRL hormone. This is considered a result of the psychological and neurological effect on women suffering from polycystic ovary syndrome. The presence of a positive relationship between the high level of PRL in women suffering from polycystic ovary syndrome and insulin resistance has increased disturbances in ovulation and infertility [27,28]. indicated that a significant increase in hormone concentration may be due to pathological causes, including polycystic ovary syndrome and hypothyroidism.

The study results, as shown in Table (2), revealed a significant increase (P≤0.05) in FSH levels. FSH, the primary hormone during the follicular phase of the menstrual cycle, is essential for egg development and maturation, leading to estrogen secretion from the mature Graafian follicle [29]. Conversely, LH, which is dominant in the luteal phase, stimulates ovulation and progesterone production in the corpus luteum. Imbalances in FSH and LH levels affect progesterone, estrogen, and testosterone, disrupting ovarian reproductive functions [30]. Disruption in the hypothalamic-pituitary axis results in increased pulsatile release of LH, causing an LH to FSH ratio greater than 2.5, as noted in studies [31,32]. This imbalance prevents ovulation and leads to ovarian cyst formation, causing delayed menstruation or fertility issues [33]. This increase is due to the ovary's

failure to secrete gonadotropins like estrogen, influenced by negative feedback mechanisms.

The elevated LH levels are attributed to a dysfunction in the hypothalamus, which causes an abnormal increase in the frequency of gonadotropin-releasing hormone (GnRH) pulses. This rapid and intensified pulsation leads to increased secretion of the LH hormone [33].In PCOS syndrome, more than A single ovarian follicle begins to grow, and a large group of them reach different stages of maturation, which leads to the accumulation of large numbers of follicles. However, most of them have not entered their final stages of maturation, and these in turn contain in their histological composition the theca cells that mainly produce androgens and which do not suffer from From the process of converting its chemical structure to estrogen to disturb the concentration or level of follicle-stimulating hormone in the serum [34].

The disorders and imbalances resulting from polycystic ovary syndrome have created an imbalance between oxidants and their antioxidants, Table No. (3). Oxidation processes occur when oxygen free radicals interact with molecules in living tissues and cells, creating additional free radicals. While these reactions are a normal part of physiological processes, they can become damaging under pathological conditions, resulting in oxidative damage [35]. Research has shown that free radical production increases in diseases such as cancer, diabetes, and chronic heart conditions [36]. These radicals mainly target biomolecules like lipids, proteins, and nucleic acids [37], causing DNA fragmentation, attacking polyunsaturated fatty acids, and leading to cellular membrane damage through lipid peroxidation [38,39]. When fatty acids are oxidized, these substances are broken down to form a short-chain compound called malondialdehyde (MDA) [40]. Hyperinsulinemia is also responsible for an increase in ROS, which are the active oxygen species, thus causing insulin resistance and hyperandrogenism, and ROS is formed in response. In women with polycystic ovary syndrome (PCOS), elevated reactive oxygen species (ROS) levels have been observed in both obese and lean individuals [41]. Our findings align with other studies indicating that increased oxidative stress linked to obesity is associated with insulin resistance[42].

The uncontrolled production of free radicals is taken into consideration as an important factor in tissue destruction in some cases. Other studies have also shown that oxidative stress directly stimulates hyperandrogenism. Other studies have confirmed that oxidation stimulates the ovaries to increase the secretion of androgens, while an increase in antioxidants such as GSH and glutathione work. To suppress its secretion [43], a study also showed that the theca cells in ovarian tissue can be stimulated by sugar to produce oxidation factors that stimulate hyperandrogenism [44]. All therapeutic methods for reducing androgenism contribute to Reducing oxidative stress by raising antioxidants that suppress the harmful role of oxidation. Glutathione (GSH) is one of the defense mechanisms in the body. It plays an important role as an antioxidant that tries to reduce damage from every high-stress situation. It works to scavenge and suppress the forms of free radicals and resist their negative effects [13].Oxidative stress is an imbalance between oxidants and their antioxidants and the generation of active oxygen species. Therefore, people with PCOS have an increase in oxidant substances, especially the concentration of malonidealdehyde (MDA), which is a stimulating factor in causing the disease compared to those without those infected [45]. Polycystic ovary syndrome (PCOS) is associated with an increase in malondialdehyde (MDA) levels, which rise in 47% of women with PCOS. This finding aligns with the study by [46], which reported significant differences in MDA concentrations between the study group and the control group. Specifically, serum MDA levels were notably higher in PCOS patients compared to controls, and patients with a body mass index greater than 40 kg/m² exhibited higher MDA concentrations compared to those with a lower body mass index. The level of GSH was significantly decreased in patients with polycystic ovary syndrome compared to the control group, and that low GSH

levels may be indirectly related to insulin resistance, and low levels of GSH may be a result of increased glucose utilization under hyperglycemic conditions [47].

In PCOS patients, impaired mitochondrial function is indicated by reduced oxygen consumption in mitochondria, which leads to decreased levels of glutathione (GSH) and a compromised plasma membrane potential [48].

The current study's findings align with those of [49] concerning catalase levels. The observed decrease in catalase (CAT) activity may be attributed to increased production of lipid peroxides and elevated concentrations of malondialdehyde (MDA), which can lead to the inactivation of many enzymes associated with the plasma membrane, and it may be An increase in circulating lipid peroxides is related to a deficiency of SOD in body tissues, and a decrease in CAT activity can also be due to enzyme depletion due to an increase in oxidative stress.

While the results of the current study differ with the results of the study of [50], which indicated that CAT activities were significantly higher in patients with polycystic ovary syndrome (PCOS) compared to the control group, and its activities were related to Cholesterol and LDL-C in the PCOS group, it was also observed that a similar trend was present in patients with this syndrome, showing an inverse relationship between malondialdehyde (MDA) levels and catalase (CAT) activity. The balance between active oxygen radicals and antioxidants greatly affects reproductive activities, such as changes in the uterine lining in different luteal phases, folliculogenesis, ovulation, fertilization, reproduction, placental growth and embryogenesis [51], however Under conditions of oxidative stress, reproductive and fertility impairment may occur, including poor ovarian function, deterioration in the quantity of eggs, and growth disorders. It has been noted that antioxidants have an important role in the functions of the female reproductive system, so polycystic ovary syndrome is associated with a decrease in the concentration of antioxidants, and this increases Oxidative stress [52,53]

4. Conclusion

The results of this study are consistent with [54], which found that there are no significant differences between the study group and the control group in SOD concentration. Although the decrease in SOD activity does not have any effect on the fertilization rate or embryo quality, SOD activity in the serum can be a parameter. Clinically, to assess systemic oxidative stress in polycystic ovary syndrome (PCOS), the findings of this study contrast with those of [45], which reported elevated serum levels of superoxide dismutase (SOD) in PCOS patients. The abnormal oxidative stress indicators in women with PCOS, regardless of their weight, suggest that oxidative stress might play a role in the pathophysiology of this prevalent condition.

REFERENCES

[1] Hylactou M, Clarke SA, Patel B (2020). Clinical and biochemical discriminants between functional hypothalamic amenorrhoea (FHA) and polycystic ovary syndrome (PCOS). Clin Endocrinol (Oxf). 2020;95:239-252.

[2] Akanksha Garg, Bijal Patel, Ali Abbara, and Waljit S. Dhillo (2022). Treatments targeting neuroendocrine dysfunction in polycystic ovary syndrome (PCOS). Clinical Endocrinology; 1–9.

[3] Jia Qi (2018). Local Cortisol Elevation Contributes to Endometrial Local Cortisol Elevation Contributes to Endometrial. The Journal of Clinical Endocrinology & Metabolism, 103(7): 2457–2467.

[4] Tiantian Zhu & Mark Goodarzi (2022). Causes and Consequences of Polycystic Ovary Syndrome: Insights From Mendelian Randomization. The Journal of Clinical Endocrinology & Metabolism, 107(3): e899–e911.

[5] Homburg R (2002). What is polycystic ovarian syndrome? A proposal for a consensus on the definition and diagnosis of polycystic ovarian syndrome. Hum Reprod; 17-9.

[6] Miya Ismayilova & Sanni Yaya (2022). "I felt like she didn't take me seriously": A multi-methods study examining patient satisfaction and experiences with polycystic ovary syndrome (PCOS) in Canada. Ismayilova and Yaya BMC Women's Health, 22:47.

[7] McArdle D, Katchl (2000). Essentials of exercise physiology 2nd Ed. Philadelphia: Lippincott Williams Wilkins, (38).

[8] Tietz (2006). Textbook of Clinical Chemistry and Molecular Diagnostics, 4th Edition. Elsevier Saunders Publishers, pp. 2021-2027.

[9] Lenton E, Meal L, Sulaiman R (1982). Plasma concentrations of Human Gonadotropin from the Time of Implantation until the second week of pregnancy. Fertility and Sterility, 37:773-778. Little Brown, NY.

[10] Vitt UA, Kloosterboer HJ, Rose UM, Mulders JW, Kiesel PS, Bete S, Nayudu PL (1998). Isoforms of human.

[11] Guidet B, Shah S (1989). A practical guide to the assessment of ventricular diastolic pre. Am J Physiology, 257(26):440.

[12] Hadwan MH, Kadhum Ali S (2018). New spectrophotometric assay for assessments of catalase activity in biological samples. Analytical Biochemistry, 1;542:29-33.

[13] Al-Zamely, Mizil YO, Al-Nimer MS (2001). Detection the level of peroxynitrite and related with antioxidants status in the serum of patients with acute myocardial infarction. National J of Chemistry, (4): 625–637.

[14] Zhang C, Bruins ME, Yang ZQ, Liu ST, Rao PF (2016). A new formula to calculate the activity of superoxide dismutase in indirect assays. Analytical Biochemistry, 503:65-67.

[15] Sahu, Nazhan Muhammad, et al. (2021). Statistics: Mathematical Applications. Dar Al-Resala Printing, 1st edition, Iraq.

[16] Pasquli R, Pelusi C, Genghini S, Cacciari M, Gambineri A (2003). Obesity and reproductive disorders in women. J. Hum. Repro; 9-35-72.

[17] Jedel E, Waern M (2010). Anxiety and depression symptoms in women with polycystic ovary syndrome compared with controls matched for body mass index. Hum Reprod, 25(2): 450-456.

[18] Recabarren SE, Smith R (2008). Metabolic profile in sons of women with Polycystic Ovary Syndrome. J. Clin. Endocrinal. Metal., 93(5):156-81.

[19] Arita MK (2001). Regression of both pituitary and ovarian cysts after administration of thyroid hormone in a case of primary hypothyroidism. Internal Medicine, 40:751-55.

[20] NHS Natural Health Solutions for PCOS (2004). Hypothyroidism and PCOS. Nancy Ounne, Naturopathic Physician, Bill Slater.

[21] Loverro G, Lorusso F, Mei L, Depalo R, Cormio G, Selvaggi L (2002). The plasma homocysteine levels are increased in polycystic ovary syndrome. Gynecologic and Obstetric Investigation, 53:157-162.

[22] Kim YW, Kim JY, Park YH, Park SY, Won KC, Choi KH, Huh JY, Moon KH (2006). Metformin restores leptin sensitivity in high-fat-fed obese rats with leptin resistance. Diabetes, 55:716-24.

[23] Sepilian VP, Crochet JR, Nagamani M (2006). Serum soluble leptin receptor levels and free leptin index in women with polycystic ovary syndrome: relationship to insulin resistance and androgens. Fertil Steril, 85:1441-1447.

[24] Porter MB, Brumsted JR, Sites CK (2000). Effect of prolactin on follicle stimulating hormone receptor binding and progesterone production in cultured porcine granulosa cell. Fertil. Steril., 73(1):99-105.

[25] Panzan MQ, Junior JM, Damotta EL, Haapalainen EF, Dejesus Simoes M, Baptista HA, Haidar MA, Baracat EC (2006). Metoclopramide-induced hyperprolactinemia caused marked decline in pinopodes and pregnancy rates in mice. Hum. Reprod., 21:2514-2520.

[26] Vale W, Wiater E, Gray P, Harrison C, Bilezikjian L, Choe S (2004). Activins and Inhibins and Their Signaling. Ann NY Acad Sci, 1038:142-147.

[27] Altuntas CZ, Johnson JM, Tuohy VK (2006). Autoimmune targeted disruption of the pituitary-ovarian axis causes premature ovarian failure. J. Immunol., 177(3):1988-96.

[28] Sharquic KE, AL-Bayatti AA, AL-Ajeel AI, AL-Bahar AJ, AL-Nuaimy AA (2007). Free testosterone, luteinizing hormone, follicle-stimulating hormone ratio in patients with Polycystic Ovary Syndrome. Saudi Med, 28(7):1039-43.

[29] ASRM (American Society for Reproductive Medicine) (2007). Patient fact sheet: Hyperprolactinemia. Highway, Birmingham, Alabama 35216-2809. www.asrm.org.

[30] Banaszewska B, Spaczyński RZ, Pelesz M, Pawelczyk L (2003). Incidence of elevated LH/FSH ratio in polycystic ovary syndrome women with normo- and hyperinsulinemia. Annales Academiae Medicae Bialostocensis, 48:132-134.

[31] Adil F, Ansar H, Munir AA (2005). Polycystic ovarian syndrome and Hyperinsulinemia. J. Liaqat Uni Med Health Sci, 4(3):89-93.

[32] Agarwal A, Gupta S, Sharma R (2005). Oxidative stress and its implications in female infertility: A clinician's perspective. Reprod Biomed Online, 11(5):641-50.

[33] Sheu JY, Tseng WC, Chen MT (2003). Determination of thiobarbituric acid of Malondialdehyde using on-line microdialysis coupled with high-performance liquid chromatography. Analytical Sciences, 19:621-624.

[34] Badizadegam (2003). Cell injury, adaptation, and death. Harvard MIT Division of Health Science & Technology, HST.035.

[35] Espey MG, Miranda KM, Thomas DD, Zavier S, Citrin D, Vitek MP, Wink DA (2002). A chemical perspective on the interplay between NO, reactive oxygen species, and reactive nitrogen oxide species. Ann NY Acad Sci, 962:195-206.

[36] Mishra J, Srivastava SA, Shukla A, Raghav CSR (2007). Antioxidants in aromatic and medicinal plants: Modulating in vivo activity. Sci Tech, pp. 1-16.

[37] Block C, Dietrich M, Norkus E, Morrow JD, Poker (2002). Factors associated with oxidative stress in human populations. Am J Epidemiol., 156(3):274-278.

[38] Gonzalez F, Rote NS, Minium J, Kirwan JP (2006). Reactive Oxygen species-induced oxidative stress in the development of insulin resistance and hyperandrogenism in polycystic ovary syndrome. J Clin Endocrinol Metab, 91(1):336-340.

[39] Sabuncu T, Vural H, Harma M, Harma M (2001). Oxidative stress in polycystic ovary syndrome and its contribution to the risk of cardiovascular disease. Clin Biochem, 34(5):407-13.

[40] Nisenblat V, Norman RJ (2009). Androgens and polycystic ovary syndrome. Curr Opin Endocrinol Diabetes Obes, 16(3):224-31.

[41] Piotrowski P, Rzepczynski I, Kwintkiewicz J, Dule

[42] ba AJ, Woodruff TK (2005). Oxidative stress induces expression of activin A in rat preovulatory follicles. Endocrinology, 146:1904-1911.

[43] Chappell LC, Seed PT, Briley A, Kelly FJ, Lee R, Hunt BJ, Parmar K, Bewley SJ, Shennan AH, Steer PJ, Poston L (2002). A longitudinal study of biomarkers of oxidative stress and antioxidant status in women with preeclampsia. Am J Obstet Gynecol, 187(1):127-36.

[44] Steiber K, Kerner J, Hoppel C (2004). Carnitine: a nutritional supplement with functional effects. J Nutr Biochem, 15: 641-649.

[45] Cohen G, Kim M, Ogwuagor N (1996). Increased interleukin-1 protein in the rat. Biochem Pharmacol., 52(1):127-9.

[46] Mishra J, Mishra MP, Srivastava AK, Raghav CSR (2008). Oxidative stress and obesity, clinic-pathological aspect. J Nutr., 7(1):30-34.

[47] Shearer WT, Reuben JM, Mullington JM, Price NJ, Lee BN, Smith EO, Szuba MP, Van Dongen HP, Dinges DF (2001). Soluble TNF alpha receptor 1 and IL-6 plasma levels in humans subjected to the sleep deprivation model of spaceflight. J Allergy Clin Immunol., 107(1):165-70.

[48] Fruzzetti F, Perini D, Russo M, Bucci F, Perrone G, Ghiadoni L, Mercuri A, Nannipieri M, Simoncini T (2023). Mechanisms of endothelial dysfunction in women with polycystic ovary syndrome: Focus on metabolic risk factors and therapeutic implications. Expert Rev Endocrinol Metab, 18(1): 15-23.

[49] Selvin E, Manzi J, Stevens LA, Coresh J, Levey AS, Greene T, Van Lente F (2007). Calibration of serum creatinine in the National Health and Nutrition Examination Surveys (NHANES) 1988-1994, 1999-2004. Am J Kidney Dis, 50:918-926.