Evaluation of the level of Secretoneurin and some biochemical variables in the blood sera of patients with polycystic ovary syndrome in the city of Samarra

Israa Ali Khalaf Al-Abbasi[1*], Ali Khudheyer Obayes[2] , and Omar Thaer Jawad[1]
[1] Department of Pathological Analysis - Faculty of Applied Sciences - Samarra University, Iraq
[2] Department of Biology- Collage of Education for Women - Kirkuk University - Iraq

*Correspondence:
usach23002@uosamarra.edu.iq

ABSTRACT

The study was conducted on 80 samples, 40 samples from patients with polycystic ovary syndrome (G1) and 40 samples from healthy people (as a control group). Their ages ranged between (18-40) years for the period from 11/1/2023 - 1/1/2024. . From Samarra General Hospital in Salah al-Din Governorate, blood was then collected from patients and healthy people and separated by a centrifuge. Then biochemical variables were measured, which included (Secretonurin, glucose, LH, FSH, Prolactin, E2). The results of the current research showed a significant increase in each of the levels (Secretonurin peptide, glucose, LH, prolactin, and E2). In the blood serum of patients with polycystic ovary syndrome compared with the control group, there was a significant decrease in the level of (FSH) in both groups at its level, probability $P \leq 0.05$.

KEYWORDS : PCOS, Secretoneurin, FSH, glucose, LH, E2.

INTRODUCTION

Polycystic Ovarian Syndrome (PCOS), originally called Stein-Levanthal Syndrome: It is known as the most common endocrine disorder. As it affects the reproductive age group, women with this disease are characterized by an increase in the secretion of androgen and gonadotropin, and it affects up to 13% of women of reproductive age (C. Ee et al, 2021).

Polycystic syndrome represents a complex, multifactorial disorder that occurs due to some environmental factors in addition to the genetic and hormonal background (Creatsas et al, 2023). It is characterized by chronic lack or absence of ovulation (anovulation, infertility, dysfunction of functional uterine bleeding, and an excess of androgens (hirsutism and acne), and the presence of polycystic ovaries. (Jaripur et al, 2022) Polycystic ovary syndrome is associated with Cysts are associated with insulin resistance, obesity, hyperinsulinemia, high blood pressure, and dyslipidemia (Kowalska et al, 2020).

Polycystic ovary syndrome is associated with obesity in the abdominal and pelvic area, insulin resistance, and metabolic disorders, as its main symptoms are high androgen levels, ovarian dysfunction, and high levels of luteinizing hormone as a result of an increase in the pituitary gland's secretion of gonadotropin-releasing hormone. In addition, the percentage of women affected by the syndrome Polycystic ovary syndrome is approximately 6-10% of women around the world, and the symptoms of this polycystic ovary syndrome appear during the teenage years and early adulthood (Azziz., 2016 & Witchell., 2019).

The treatment of polycystic ovary syndrome depends on the symptoms accompanying the patient. Sometimes oral contraceptives that contain estrogen and progesterone are the preferred medical treatment because

they improve both menstrual disorders and androgen excess. Also, exercise is very important to reduce the diseases associated with obesity and insulin resistance (Sohail et al, 2004).

Secretoneurin (SN) is a neuropeptide containing 33 to 34 amino acids. It is found in human cells in the form of proteins called Granin, of which there are two types: Secretogranin-II and Secretogranin-III. Studies have observed that this family of proteins, especially SCG3, is found in nerve cells and endocrine glands. And the hypothalamus, pancreatic beta cells, and insulin secreting cells (Stridsberg M, et al 2008), The physiological function of SCG3 is to regulate the biogenesis of secretory granules for active peptides, growth factors, and hormones (Bartolomucci A, et al 2011). It was noted that it has an effect on insulin secretion. SCG3 also had some roles in assisting insulin processing, which affects glucose balance (Maed Yet al, 2018 & Dowling P et al, 2008). Some recent studies indicate that serum SCG3 concentrations are higher in people with metabolic syndrome (Lin CC et al, 2019).

In addition, the female reproductive system is controlled by several basic hormones, which include the hypothalamus, pituitary gonadotropins, and gonadal sex hormones. The reproductive cycle is the result of the coordination of all these hormones (F. L. Saleh et al, 2023), Hormones are chemical messengers, secreted in response to specific stimuli. They are released from one organ and transported through the bloodstream to another organ (the target organ), where they initiate a specific cellular reaction. The female hormonal system consists of three sequential hormones as follows: The hormone released from The hypothalamus is the gonadotropin releasing hormone (GnRH). Sex hormones are from the anterior lobe of the pituitary gland and include follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which are secreted as a result of the stimulation of hormones released from the hypothalamus (GnRH)(A. Christensen et al, 2022). In addition to the ovarian hormones, estrogen and progesterone, which are secreted from the ovary in response to the hormones secreted from the anterior pituitary. (Bosch E et al, 2021) Through the rise in secretoneurin peptide and sex hormones, the current research aims to evaluate the level of secretoneurin along with some biochemical variables in the patients' blood serums. Women with polycystic ovary syndrome in the city of Samarra.

MATERIALS AND METHODS
• Collection of specimens

The study was conducted on 80 samples, 40 samples from patients with polycystic ovary syndrome and 40 samples from healthy people (as a control group), whose ages ranged between (18-40) years for the period from 11/1/2023 - 1/1/2024. From Samarra General Hospital in Salah al-Din Governorate, blood was then collected from patients and healthy people. After that, blood was collected from patients and healthy people and was separated by a centrifuge. Then the required biochemical variables were measured.

• Estimating the level of hormones in blood serum

The hormone examination included (Secretonurin, LH, FSH, Prolactin, E2).It is based on the competitive principle. When samples are added to pits covered with hormone antibodies, the enzyme will compete with the hormone antibodies present in the samples to bind to the antibodies and the concentration of the enzyme bound to the pits decreases, as the concentration of hormones in the sample increases and the enzyme not bound to the washing process is removed, TMB solution is added and incubated for a specific period to produce a blue color change. After that, the reaction is stopped by adding the stop solution and the absorbance of the samples is read at a wavelength of 450 nm. These hormones were measured in blood serum, according to the company. Manufacturer: Monobind Inc, USA. Using the ELISA test method, using a measuring kit for each measurement.

• Estimating the level of glucose in blood serum

The level of glucose in blood serum was measured by the Spanish company BioSystems, using an assay kit prepared using the enzymatic method followed by (Young 2001).

Statistical analysis

The results were analyzed using the statistical program SPSS, and the mean and standard deviation ± SD value were determined, as well as the averages were determined for the group with polycystic ovary syndrome compared to the control group using the T-test and at the probability level (P ≤ 0.05).

RESULTS AND DISCUSSION

The results showed a significant increase in each of the levels (secretonurin peptide, glucose, LH, prolactin, and E2). In the blood serum of patients with polycystic ovary syndrome compared with the control group, there was a significant decrease in the level of (FSH) in both groups at its level, probability P ≤ 0.05, as in Figures (1,2,3,4,5,6), respectively.

Table No. (1) shows the mean ± standard deviation of the biochemical variables for the samples under study

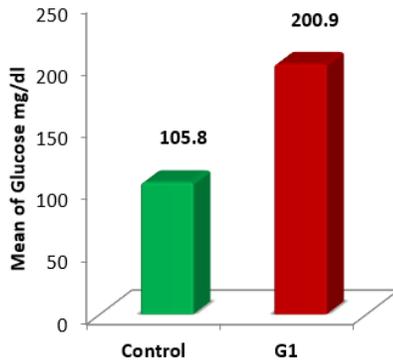| Parameter	Groups (Mean ± SD)		P-Value
	Control (n=40)	Patients (n=40)	
Secretoneurin(ng/ml)	11.83± 1.94	57.2 ± 22.0	P ≤ 0.05
Glucose (mg/dl)	105.8± 10.1	200.9± 33.9	P ≤ 0.05
LH(mIU/ml)	2.98±18.55	39.87 ±8.49	P ≤ 0.05
FSH(mIU/ml)	29.58 ± 5.18	14.27±3.15	P ≤ 0.05
E2(pg/ml)	90.6 ± 11.6	283.5± 59.7	P ≤ 0.05
Prolactin (ng/ml)	8.80 ± 1.54	32.29 ±4.85	P ≤ 0.05

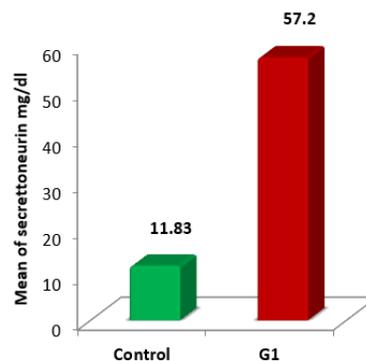Figure (1): - Secretoneurin in the blood serum of the samples under study

Figure (2): - Glucose in the blood serum of the samples under study
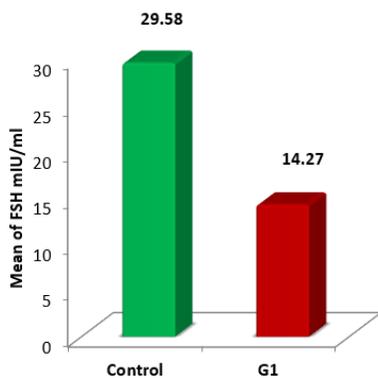

Figure (3): - LH in the blood serum of the samples under study
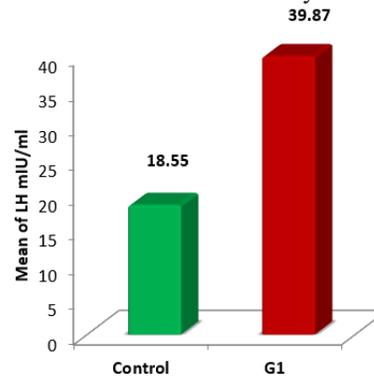

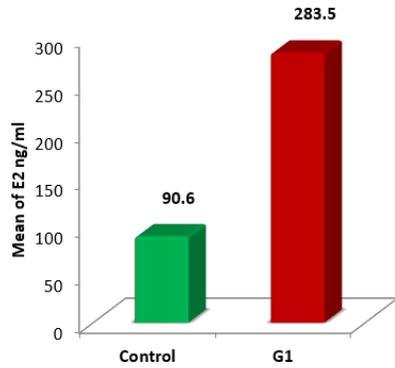Figure (4): - FSH in the blood serum of the samples under study

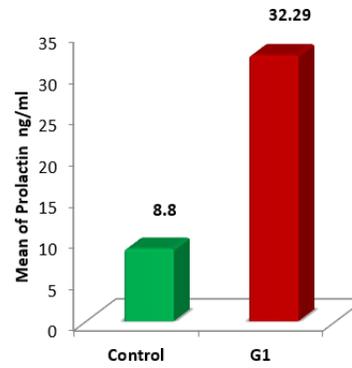Figure (5): - E2 in the blood serum of the samples under study

Figure (6): - Prolactin in the blood serum of the samples under study

The continuous increase in the level of glucose leads to a defect in cellular functions and the occurrence of several diseases such as diabetes, obesity, and polycystic syndrome. The increase in the level of the neuropeptide secretoneurin in patients with polycystic ovary syndrome may be attributed to an increase in many hormones directly related to metabolism. The body, such as obesity in the abdominal area, high blood pressure, and insulin resistance (Talbott et al., 2001), as insulin resistance is a common symptom of polycystic ovary syndrome (Essach et al., 2007).

The literature has not indicated a study on the hormone secretoneurin and its relationship to polycystic ovary syndrome. Therefore, in addition to that, the reason for the increase in the hormone Secretoneurin may be due to high levels of sex hormones, which leads to hormonal disturbance and thus the absence of ovulation. The pituitary gland and hypothalamus are among the main organs that regulate The mechanism of action of the endocrine system (Herman et al., 1996). In the anterior lobe of the pituitary gland, the portal system works to produce peptides that bind to specific receptors located on the surfaces of cells, and thus they either work to inhibit inhibiting hormones or release hormones (Haisenleder et al., 1991). Since polycystic ovary syndrome is affected by the increased secretion of some hormones and the decreased secretion of others, there is a need for more studies on the relationship of secretoneurin and its relationship to polycystic ovary syndrome.

As for the glucose level, its increase may be due to excessive secretion in the level of prolactin, which leads to the development of disorders in glucose and insulin metabolism, as patients who suffer from polycystic ovary syndrome commonly suffer from an imbalance in blood sugar after eating, which increases the risk of developing type diabetes. The second, especially in obese women (Rosenfield and Kakoly., 2018, 2016).

Morin-Papuner et al (Morin-Papuner, 2000) have pointed out that an increase in glucose secretion in the blood indicates a defect in the secretion of the hormone insulin, and this is an indication of the presence of insulin resistance, which is directly related to a high level of glucose in the blood. It has also been found that a defect in insulin action in women with polycystic ovary syndrome has a limited effect on the process. Metabolism of blood glucose (Dunaif., 1995). Insulin resistance in PCOS occurs due to impaired insulin action in various target tissues, which is characterized by primary compensatory hyperinsulinemia and decreased insulin response to hyperglycemia, as PCOS affects the majority of organ systems and tissues in the body (Diamanti-Kandarakis, 2012).

As for the LH hormone, its results agreed with the results of the study (Hussain., 2021) (Jadav., 2020), which indicated in their study an increase in the level of luteinizing hormone in the blood serum of patients with polycystic ovary syndrome compared to healthy women, as it reinforces the reason for the resulting increase in The presence of an ovarian defect (hypo- or hypergonadism) and may also occur as a result of psychological stress or an imbalance in the diet (Henríquez., 2020).

The results of (Taleb, 2022) also indicated that women with secondary infertility and polycystic ovary syndrome have an increase in the level of luteinizing hormone, as it was found that the most common clinical symptom in patients with polycystic ovary syndrome is an increase in the LH/FSH ratio, as the LH level is higher than the FSH level. Which leads to an increase in the rate, an increase in androgens in the ovary, and a failure in the ovulation

process (N. A. Malini., 2018), Therefore, an increase in the level of luteinizing hormone leads to a defect in the ovulation process or the absence of ovulation in the follicular cycle, as the luteinizing hormone stimulates ovulation and then stimulates the corpus luteum to form steroid hormones, but a high level of it inhibits the effectiveness of aromatase and inhibits the growth of the oocyte (Al-Jubouri, 2014). While Hasan, 2020, indicated that the diagnosis of polycystic ovary syndrome has the best sensitivity and specificity when the LH/FSH ratio is greater than (Hasan et al., 2020).

As for the FSH hormone, the results of his study do not agree with the results of (Salman), who indicated in his study that there are no significant differences in the level of follicle-stimulating hormone in the blood serum of women with polycystic ovary syndrome. The slight decrease in the hormone level may be due to the fact that a high concentration of prolactin may inhibit the secretion of FSH hormone (Eldar-Geva., 2001) Melmed et al 2004 also indicated that the decrease in the hormone level may be due to the production of adrenaline from the adrenal gland, which in turn affects the concentration of FSH through the secretion of androgens.

As for the E2 hormone, its increase is due to an increase in blood insulin in the body, which helps stimulate the synthesis of steroids, in addition to the role of high androgens, which generate pressure on stimulating the expression of aromatase in adipose tissue, which participates in the construction of estrogen and the metabolism of androgens, and thus metabolism is involved with polycystic ovary syndrome because they are linked to increased metabolism. Androgens and increased blood insulin (Shaaban et al., 2019).

It has been found that estrogen mediates vital effects in the reproductive system of women, preserves reproductive functions, and has many functions in the body through hormone receptors spread in the nuclei, cytoplasm, and mitochondria of cells. There is research indicating that abnormal estrogen affects the growth and development of follicles. However, more understanding of the role of estrogen in Polycystic ovary syndrome (Xu et al., 2021). The abnormal secretion of estrogen during the follicular stage, whether it increases or decreases, and in most cases there is an increase in estrogen secretion due to a lack of progesterone as well as the effect of androgens, especially women who suffer from obesity and an increase in visceral adipose tissue, which works to increase the luteinizing hormone (AL-juaifari). 2020).

As for the hormone prolactin, we notice from the results an increase in prolactin levels in women with polycystic ovary syndrome compared to healthy women, and that this increase in hormone levels is the main cause of irregular menstruation, as it causes a disturbance in the luteal phase, which leads to a lack of ovulation and an irregular menstrual cycle. If it rises to very high levels, it may lead to cessation of the menstrual cycle (Micheal, 2002. The cause of high prolactin is due to the use of medications that increase the concentration of the hormone in the blood. It may increase the concentration of the prolactin hormone above the normal level in patients with polycystic ovary syndrome in order to increase the stimulation of lactotrophs, which are responsible for producing the hormone from the anterior lobe of the pituitary gland, which leads to an increase in its secretion, and its increase is linked to Women always secrete milk, which has been observed in some women with polycystic ovary syndrome (Nader., 2010).

CONCLUSIONS

From the current research, we conclude the following scientific facts, We conclude from the current research that there was a significant increase in each of the levels (Secretonurin peptide, glucose, LH, Prolactin, and E2). In the blood serum of patients with polycystic ovary syndrome compared with the control group, at a probability level of $P \leq 0.05$. There was a significant decrease in the level of (FSH) in the blood serum of patients with polycystic ovary syndrome compared to the control group, and at its level the probability of $P \leq 0.05$.

.

REFERENCES

A. Christensen *et al.*, "Horm. Metab. Res.," *NIH Public Access Author Manuscr.*, vol. 44, no. 8, pp. 587–591, 2020, doi: 10.1055/s-0032-1306301.Hormonal.

Al-juaifari, B. A. J., and Al-jumaili, E. F. (2020). Correlation of Body Mass Index and Some Hormones (Estradiol , Luteinizing , Follicle Stimulating Hormones) with Polycystic Ovary Syndrome among Young Females [20 to 35 Years]. 13(March), 193–198.

Al-Jubouri meeting Hassoun. A physiological study of polycystic ovary syndrome in Kirkuk Governorate, doctoral thesis, College of Science, Kirkuk University, 2014.

Azziz, R..; Carmina, E.; Chen, Z.*et al*. Polycystic ovary syndrome. Nature reviews Disease primers.2016; 2(1): 1-18.

Bosch E, et al., Reduced FSH and LH action: implications for medically assisted reproduction. Hum Reprod. 2021 May 17;36(6):1469-1480. doi: 10.1093/humrep/deab065. PMID: 33792685; PMCID: PMC8129594.

C. Ee, S. Pirotta, A. Mousa, L. Moran, and S. Lim, "Providing lifestyle advice to women with PCOS : an overview of practical issues affecting success," pp. 1–12, 2021.

Creatsas and E. Deligeoroglou, "Polycystic ovarian syndrome in adolescents," *Curr. Opin. Obstet. Gynecol.*, vol. 19, no. 5, pp. 420–426, 2023, doi: 10.1097/GCO.0b013e3282efdc54.

Dunaif, A. Hyperandrogenic anovulation (PCOS): a unique disorder of insulin action associated with an increased risk of non-insulin-dependent diabetes mellitus. The American J of medicine.1995; 98(1): 33-39.

E. Diamanti-Kandarakis and A. Dunaif, "Insulin resistance and the polycystic ovary syndrome revisited: An update on mechanisms and implications," *Endocr. Rev.*, vol. 33, no. 6, pp. 981–1030, 2012, doi: 10.1210/er.2011-1034.

Eldar-Geva, T.; Spitz, I. M.; Groome, N. P.; Margalioth, E. J. and Homburg, R. Follistatin and activin A serum concentrations in obese and non-obese patients with polycystic ovary syndrome. Human reproduction.2001; 16(12): 2552-56.

Essach, P. A; Wickham E P & Nestler J. E. (2007). The metabolic Syndrome in polycystic ovary Syndrome Clinical Obstetrics and Gynecology, 50: 205-225.

F. L. Saleh and H. S. Taylor, "Clinical applications of gonadotropin-releasing hormone analogues: a broad impact on reproductive medicine," *F&S Reports*, vol. 06520, pp. 1–5, 2023, doi: 10.1016/j.xfre.2023.01.008.

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.

Hasani, "Glucose transporters in adipose tissue, liver, and skeletal muscle in metabolic health and disease," *Pflugers Arch. Eur. J. Physiol.*, vol. 472, no. 9, pp. 1273–1298, 2020, doi: 10.1007/s00424-020-02417-x.

Herman, JP.; Prewitt, CM. and Cullinan. (1996). Neuronal circuit regulation of the hypothalamo, pituitary, adrenocortical stress axis. Crit.Rev.Neurobiol. ,10:371-394.

Hussein, Riam Ali. Evaluation of some hormones and biochemical variables in the blood of women with polycystic ovary syndrome in the city of Baghdad. Master's thesis. Tikrit University. Faculty of Science. Department of Chemistry. 2021.

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

Jaripur, H. Ghasemi-Tehrani, G. Askari, M. Gholizadeh-Moghaddam, C. C. T. Clark, and M. H. Rouhani, "The effects of magnesium supplementation on abnormal uterine bleeding, alopecia, quality of life, and acne in women with polycystic ovary syndrome: a randomized clinical trial," *Reprod. Biol. Endocrinol.*, vol. 20, no. 1, pp. 1–11, 2022, doi: 10.1186/s12958-022-00982-7.

Kakoly, N. S.; Khomami, M. B. and Joham, A. E. Ethnicity, obesity and the prevalence of impaired glucose tolerance and type 2 diabetes in PCOS: a systematic review and meta-regression. Human reproduction update.2018; 24(4): 455-467.

Kowalska, "Changes in Metabolic Profile in the Women with a History of PCOS — A Long-Term Follow-Up Study," 2020.

Melmed, S. and Jameson, L. In Harrison principes of internal medicin. New York Mc Graw Hill Professional.2004.

Micheal,; T.MC and Dermott, M.D.(2002). Hypothyrodism , Endocrine secrets , Thired Edition .Hanley & Belfus , INC.33:P:208-212.

Morin-Papuner, L.C.;Vauhkonen, I.; Koivunen, R.M.; Ruokonen, A. and Tapanainen, J.S .Insulin sensitivity, insulin secretion, and metabolic and parameters in healthy women and women with polycystic ovarian syndrome. Ilum Reprod. 2000; 15:1266 1274.

N. A. Malini and K. Roy George, "Evaluation of different ranges of LH:FSH ratios in polycystic ovarian syndrome (PCOS) – Clinical based case control study," Gen. Comp. Endocrinol., vol. 260, pp. 51–57, 2018, doi: 10.1016/j.ygcen.2017.12.007.

Nader, Reem Adib Mohamed .Study of the relationship between hormone lactation and infertility among women in the city of Tikrit and its suburbs. Thesis Masters. Faculty of Science, University of Tikrit,2010.

Rosenfield, R. L. and Ehrmann, D. A. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocrine reviews.2016: 37(5): 467-520.

Salman, Nour Younis. The effect of polycystic ovary syndrome on some biochemical variables and the oxidative stress balance among some affected women in the city of Samarra. Master's thesis. College of Education. 2022.

Shaaban, Z., Khoradmehr, A., Jafarzadeh Shirazi, M. R., & Tamadon, A. (2019). Pathophysiological mechanisms of gonadotropins- and steroid hormones-related genes in etiology of polycystic ovary syndrome. Iranian Journal of Basic Medical Sciences, 22(1), 3– 16.

Sohail, R.; Islam, N.;Zaman,F. (2004). Frequency of impaired glucose to lerance in polycystic ovarian disease . J. Surg Pakistan 9: 31- 3 .

Talbott, E.O.; Zoborowsk, J.V.; Sutton Tyrrell K, Mc Hugh-pemu Kp and, Guzick D.S (2001). Cardio vascular risk in women with polycystic ovary syndrome. Obstet Gynecol Clin North, 28:111-133.

Talib, Zahraa Rasoul. Evaluating the relationship of some metabolic biomarkers and lead with hormonal changes in women with polycystic ovary syndrome. Master's thesis. University of Karbala. College of Science. 2022.

Witchel. S. et al. An international consortium update: pathophysiology, diagnosis, and treatment of polycystic ovarian syndrome in adolescence. Hormone research in paediatrics. 2017; 88(6):371-395.

Xu, X. L., Deng, S. L., Lian, Z. X., & Yu, K. (2021). Estrogen receptors in polycystic ovary syndrome. Cells, 10(2), 1–13.

Young, D. S., & Friedman, R. B. (2001). Effects of disease on clinical laboratory tests (Vol. 1). Amer Assn for Clinical Chemistry.2001.