CANKIRI KARATEKIN UNIVERSITY
GRADUATE SCHOOL OF NATURAL AND APPLIED SCIENCES

MASTER'S THESIS

INVESTIGATION OF CLINICAL AND LABORATORY CORRELATION OF PCOS AND THYROID DISEASES

Zainab Falih Mohammed Hasan AL-KHAZAALI

DEPARTMENT OF CHEMISTRY

CANKIRI

2021

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The thesis work titled “Investigation of Clinical and Laboratory correlation of PCOS and thyroid diseases” prepared by Zainab Falih Mohammed Hasan AL-KHAZAALI was approved by the following jury unanimously on 09/07/2021, Cankiri Karatekin University Institute of Science, Department of Chemistry. It has been accepted as a MASTER'S THESIS.

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Zainab Falih Mohammed Hasan AL-KHAZALI

ABSTRACT

Master Thesis

INVESTIGATION OF CLINICAL AND LABORATORY CORRELATION OF PCOS AND THYROID DISEASES

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The most general hormonal condition among women of reproductive age is polycystic ovarian syndrome (PCOS). The common linkage between PCOS and these diverse metabolic and autoimmune diseases, primarily autoimmune thyroid illness, is well established. This study was done the period 2020-2021 in hospital of AL-IRAK. This study included 135 persons, their ages between 26- 66 year for analysis. Control group 45 healthy subjects (Group A), while Group B involved 45 patients with PCOs and, Group C including 45 Patients with PCOs and thyroid disease. The in our study have been showed that no difference significantly between the mean age in the Control group and two patients groups. LH (IU/L), FSH (IU/L), TSH (µIU/mL), testosterone (ng/mL) and LH/FSH (%) was has a significant difference between patients' groups when compared to controls group in women patients with PCOS. These biochemical markers there can be a marker to PCOs diagnosis.

2021, 64 page

KEYWORDS: PCOs, Thyroid, FSH, infertility, TSH, Testosterone

ÖZET

Yüksek Lisans Tezi

PCOS VE TIROID HASTALIKLARININ KLINIK VE LABORATUVAR KORELASYONUNUN ARAŞTIRMASI

ZAINAB FALIH MOHAMMED HASAN AL-KHAZAALI

Çankırı Karatekin Üniversitesi
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Polikistik over sendromu (PCO'lar), üreme çağındaki kadınları etkileyen en genel endokrin bozukluktur. PCOS, belirgin metabolik ve otoimmün koşullarla, baskın olarak otoimmün tiroid hastalığı ile ilişkilendirilmiştir. Bu çalışma, 2020-2021 döneminde AL-IRAK hastanesinde yapılmıştır. Bu çalışmaya analiz için yaşları 26-66 arasında değişen 135 kişi dahil edildi. Kontrol grubu 45 sağlıklı denek (Grup A), Grup B'de 45 PCO hastası ve 45 PCO ve tiroid hastalığı olan Grup C yer almıştır. Çalışmamızda control grubu ile iki hasta grubu arasında ortalama yaş arasında anlamlı bir fark olmadığı gösterilmiştir. LH (IU/L), FSH (IU/L), TSH (µIU/mL), testosterone (ng/mL) ve LH/FSH (%), kadın hastalarda kontrol grubuna göre hasta grupları arasında anlamlı farklılık gösterdi ile PCOs'dir. Bu biyokimyasal belirteçler PCO teşhisi için bir işaret olabilmektedir.

2021, 64 Sayfa

ANAHTAR KELIMELER: PCOs, Tiroid, FSH, Kısırlık, TSH, Testosterone

ACKNOWLEDGEMENTS

In the name of ALLAH, the most compassionate and the most merciful. I would like to express my gratitude and thanks to my Supervisor, Assoc. Prof. Dr. Hakan ÇOLAK and to my Co-Supervisor, Prof. Dr. Eman Mohammed for their excellent assistance, guidance and valuable suggestions during the research period.

DEDICATION

First of all, I thank God first and foremost for all that I have achieved in this life. On this occasion, I dedicate my graduation, my success and everything beautiful in my life to my father's pure spirit that still flutters in the sky of my life, I feel that his spirit is my soulmate. And my loved and patient mother, who always strengthened the energy within me and for my family especially my brother Hassan, he has been and continues to support me in every step on my life and everyone who helped me. Finally, thank you all from my heart.

ZAINAB FALIH MOHAMMED HASAN AL-KHAZAALI

ÇANKIRI, 2021.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

ECL	Electrochemiluminesvence
FSH	Follicle stimulating hormone
GnRH	Gonadotropin-releasing hormone
IU/L	International unit per liter
LH	Luteininzing hormone
Ng/ml	Nano grams per milliliter
PCOS	Polycystic Ovary Syndrome
T3	Triuodothyronine
T4	Thyroxin, Tetraiodothyronine
TSH	Thyroid stimulating hormone
TESTO	Testosterone
µIU/ml	Micro international unit per milliliter

1. INTRODUCTION

The term (PCOS) refers to the Polycystic Ovary Syndrome, Endocrine disease is the most common problem associated with premenopausal women's Endocrine disorders. Studies estimate that between 5% and 10% of women who are pregnant or attempting to become pregnant have PCOS. Most usually, the syndrome appears in adolescence, when menstruation has occurred, with symptoms of hyperandrogenism and polycystic ovarian disease. An in-depth examination of PCOS features includes hirsutism Acne, androgenetic alopecia, and the resulting reproductive problems that occur as the result of hyperandrogenism and infertility are all part of an ovulation disease. However, hypertension and hyperinsulinemia, which is regarded to have a crucial role in the pathogenesis of PCOS, have been found in PCOS patients, women with PCOS hold a maximum burden of obesity, dyslipidemia, glucose intolerance, and diabetes (Ching et al. 2007).

Polycystic ovarian syndrome may affect QoL, including infertility Also known as polycystic ovarian syndrome, hyperandrogenism causes women and gain more weight, obesity and health repercussions that go on for years. PCOS was predicted to be related to problems with the clinical inappropriate impact and health consequences on women's self-esteem and body image, as well as a progression to worsened health and quality of life, and mental illness. If that is the case, then the drug should incorporate this into the progress of the prescription for women who have been diagnosed with PCOS (Clarke et al. 2020).

PCOS impact against women probably happens in any years old during the life of the female. At first, it was hypothesized that it would mainly impact women of reproductive age due of infertility, disease has now become obvious, these conditions occur during adolescence, the early stages of the disease There are an abundance of menstrual cycles that tend to last for weeks, but regrettably this information isn't recognized or identified in this age bracket. More than likely, these young women are likely to use oral contraceptives to regulate their monthly cycles and fail to detect their infertility until much later (Cheng et al. 2020).

PCOS can effect of 5 - 10 percent of women age that they have the ability of reproductive, there are also various parameters involved in hypothyroidism in PCOS in women, some previous investigations have asserted that hypothyroidism is an insulin-resistant (IR) condition, in addition, infrared radiation is thought to be a primary cause of PCOS (Benetti et al. 2013).

When hypothyroidism case alone occurs in woman, some changes in fat metabolism occur, dysfunction, risk of arterial hypertension, endothelial, and impaired ovulation. And the same pathological symptoms happen in cases of PCOS alone (Ganie et al. 2011).

Thus, Interest in the correlation between thyroid dysfunction and PCOS has increased in recent years; However, this topic remains ambiguous, as PCOS and thyroid dysfunction are most often found together (Dittrich, et al. 2009).

This study comprises in some parts, in a first part purpose and importance of the study is mentioned. In a second part, general concepts that we deal with in our thesis are emphasized.

In the second part, Polycystic Ovary Syndrome, its epidemiology, pathology, pathogenesis, risk factors and treatment are focused on. Again, in the second part, thyroid hormone levels and effects are discussed in detail. Here, after examining the functions, synthesis, circulation and transport, mechanisms of action, effects and measurement of thyroid hormones.

This study will be one of the few ones in this field. Thus, it will be a valuable contribution to the literature.

1.1 The Aim of Study

1. It is the goal of this research to discover whether or not PCOS is connected to the thyroid gland.

2. To understand how a woman's problems are managed that may affect a woman in different ways at different times of her life (including menopause, irregular menstruation, and thyroid disorder).

3. To what extent should young women periodically undergo laboratory examination for polycystic ovaries and hypothyroidism.

2. LITRATURE REVIEW

2.1 Ovaries

In females, the two ovary-producing organs are termed ovaries to ensure a healthy reproductive system, young females must regularly undergo ova cell creation, as they are between the ages of 14 and 35 years old., oval-shaped organs about 2 - 4 cm in diameter are located on the posterior wall of the lateral pelvis of the uterus, see Figure 2.1. The length of a straight line is commonly used to measure the size of shapes or circular. It is extending from one edge of the tumor or other object, across its center and to the opposite edge (Cheong et al. 2017).

Besides their main reproductive function, the ovaries have another noteworthy distinction: they are an endocrine gland, secreting the majority of the hormones necessary for fertility and reproduction, such as estrogen and progesterone (Akrim et al. 2017).

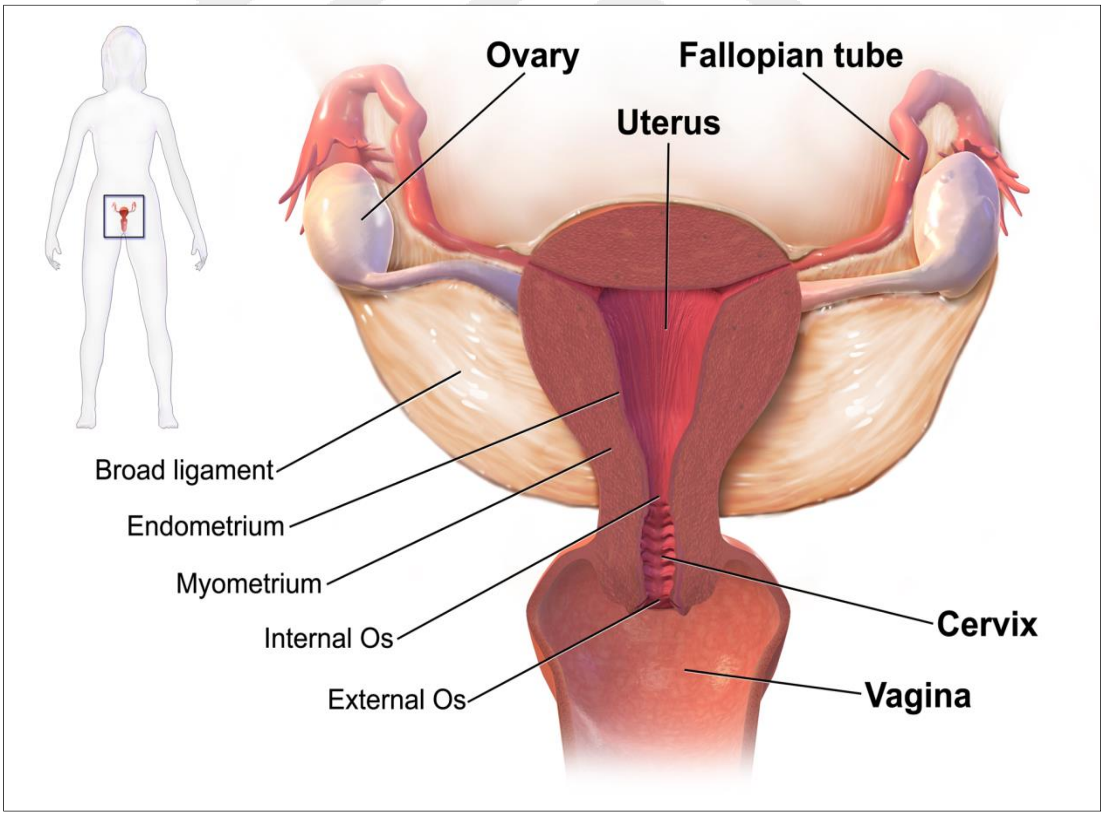

Figure 2.1 Female reproductive system, organs and structures of the female reproductive systems

2.1.1 Anatomy of the ovary

Ovaries are placed behind the pelvic organs located on either side of the uterus in front of the rectum and near the lateral pelvic wall. The anatomical and functional variations of a woman's ovaries happen as a woman moves through different stages of her life, such as during puberty, childhood, and after menopause. Ovaries are attaching with many sides inside the human female body are illustrated in below and the plotting as illustrated in Figure 2.2 (Usubutun et al. 2007; Clement, et al. 1987; McIntosh et al. 2008): -

- Appears to be connected to the abdominal wall by a double fold of ostomy on its anterior wall.

- The frequently diagnosed gripping the lateral pelvic wall to the superior portion of the lateral pole.

- On the ipsilateral (or opposite) side, both of the ovaries hook to the media (or uterine) the ovarian (or uterine) ligament.

- The ovaries of the adult women like an ovoid shape,

- The widths are 3 cm (the length of the end is 3 cm), 3 cm (the width of the middle section is 3 cm), and 0.6 cm (the thickness of the end is 0.6 cm). The weigh is 5 - 8 gm.

- Their weight and diameter are all closely correlated with their contents of follicular forces.

- During the early stages of reproduction, the egg tends to be pinkish-white in color.

- It can be recognized three main zone, these It is possible to establish three distinct zones on a sliced piece such a medulla, image input, and cortex.

- The structure of the follicular are shown in the medulla and cortex, these follicular such as; corpora lutea, cystic follicles, and corpora albicantia.

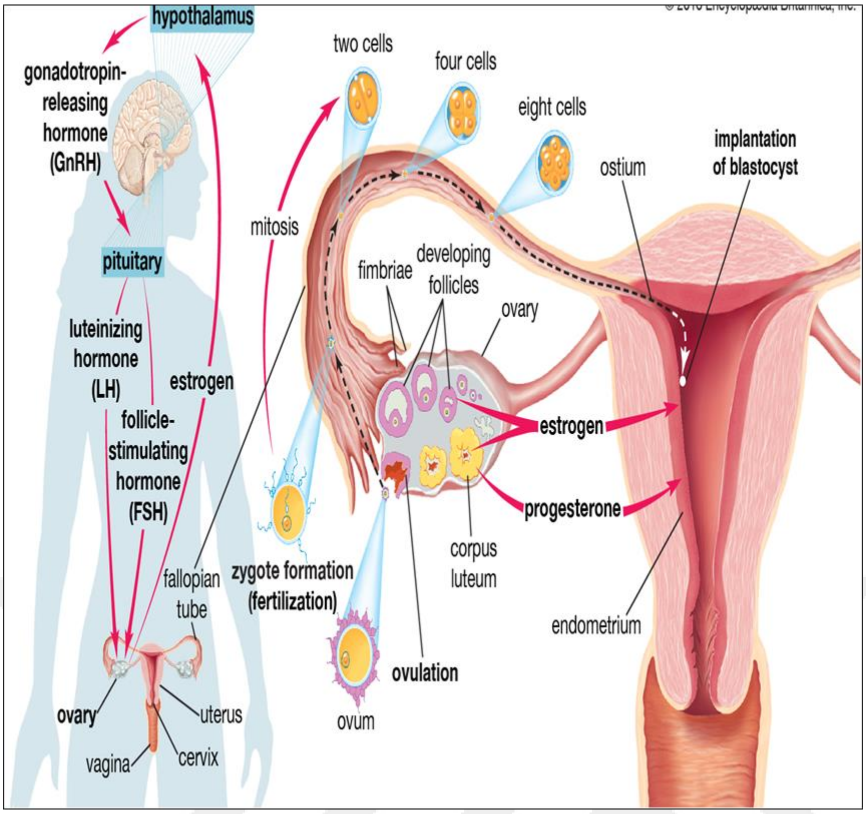

Figure 2.2 Woman's anatomy of the ovary in the reproductive age

2.1.2 Histology of the ovary

Candidacies in PCOS has been histologically defined as showing fibrous thickening of the lighter buggia and the outer cortex, polycystic lichenification with prominent thika, often with a tendency to lutein. The ovaries, which are inserted on either side of the uterus in women of reproductive age, are paired pelvic organs that are located behind the thick ligament and in front of the rectum (Clement et al. 1987).

Arterial branches originating in the sinus of Valsalva, the vertebral artery, and the superficial temporal artery anastomose to enter the oviduct and medulla via the hilum. Spiral arterioles feature longitudinal borders of internal smooth muscles, as do spiral smooth muscle arborisations. Small, straight arterioles from a plexus at the corticomedial junction make up the plexus from which the myeloid arterioles and arterioles originate. cortical arterioles arise and penetrate the cortex in a radial and circular manner so that they The ovary surfaces are parallel to each other, perpendicular to the surface. The vascular arches in the cortex are all interconnected, forming distinct groupings. In these arcades, the capillaries within the theca layers of ovarian follicles become dense networks (Erdem et al. 2002), see Figure 2.3.

A subepithelial venous plexus accompanies arterioles. The women in Anna Dulla are huge and voluptuous. Here, the veins fuse together and then funnel into the ovarian veins, which travel alongside the mesopharynx and pelvic ligament before emptying into the vena cava. The left renal vein and inferior vena cava receive the left ovarian vein's drainage, while the right ovarian vein drains into the right renal vein.

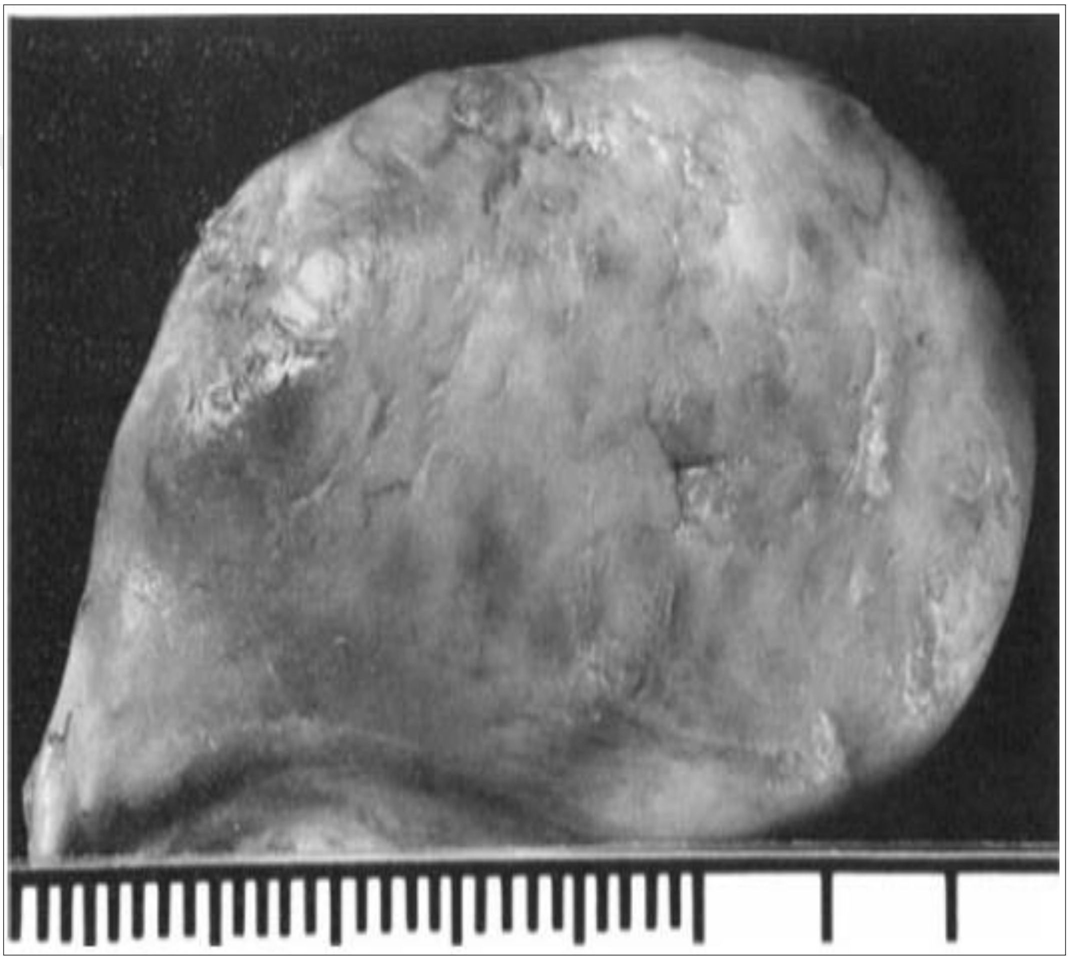

Figure 2.3 Cut surface of the normal adult ovary where occasional cystic follicles are present in the cortex

2.1.3 Ovulation

The main definition of human ovulation for a female of reproductive age is as follows, the release of one or more eggs from a female's ovaries through the ovulation process in each menstrual cycle. This is important because its male sperm cells can now fertilize the egg, allowing the embryo to be formed, and the fertilization process can occur within 24 hours after ovulation. If the egg does not receive any sperm, the menstrual period begins, usually 15 days before the next period **(**Singh et al. 2001)**.**

One egg is released at the same time in a regular menstrual cycle of a female of reproductive age, although more than one egg may be released during the menstrual cycle. During the first fourteen to sixteen days of the monthly period cycle, the egg ruptures from the ovary. This is usually the case, as the period usually occurs every four weeks (28 days), see Figure 2.4 **(**Miller et al. 2010)**.**

Oocytes that are not fertilized leave the reproductive system roughly two weeks after ovulation during menstruation. Ovulation cycles sometimes occur where the egg is not released **(**Gildersleeve et al. 2012).

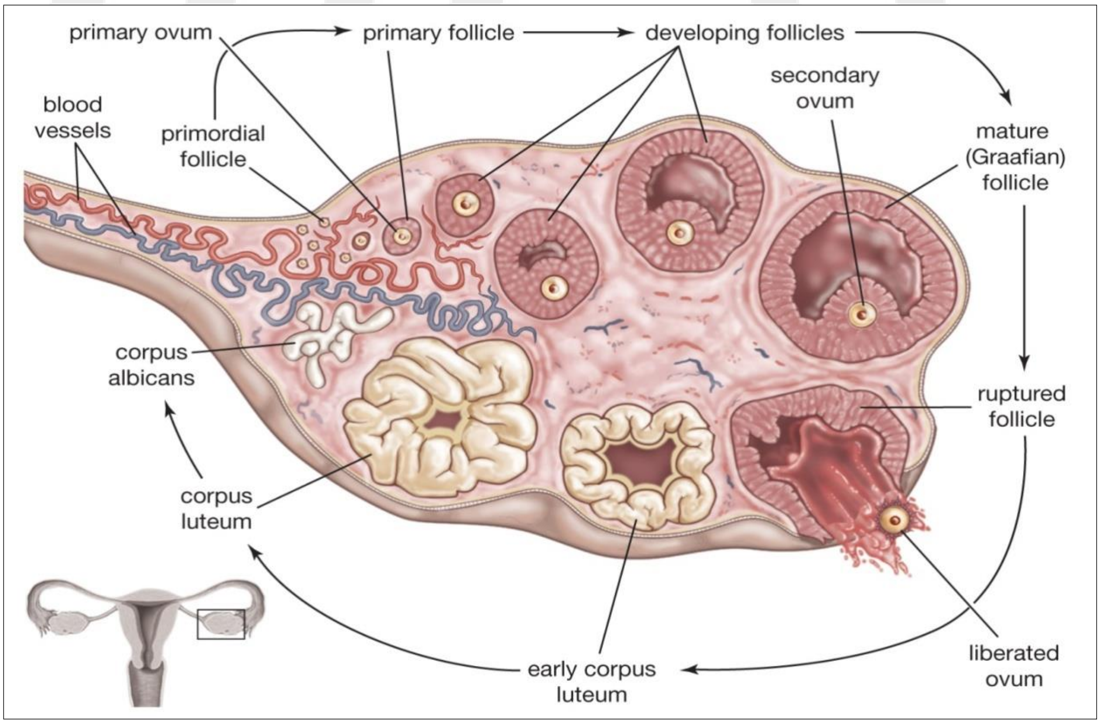

Figure 2.4 The steps of ovulation

2.1.4 Ovarian physiology, puberty period

The main definition of puberty of human female is not referring to the single event happen for both shape and function in the female body, but it is most probably referring to a single stage in development, it is not currently known what triggers puberty in time, but puberty appears to be restricted by higher controls of the central nervous system. Adolescence is the period of important physical change resulting in sexual maturity, the sexual maturation and reproductive activities The age of beginning of puberty for girls tends to be between the ages of 10.9 (Sizonenko et al. 1989).

It's normal for females to menstruate at the age of 13.4 years, and the heavier a girl is, the earlier she begins menstruating. In the human female, the first sign is breast growth. At the beginning of puberty, after a period of "quiet" the hypothalamus resumes a significant pulsating secretion of gonadotrophin-releasing hormone, the increased secretion of the pituitary gonadotropin causes a rise in the secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). These, in turn, activate the functions of the gonads. Positive feedback triggers the onset of menstruation and ovulation in girls mid or later into puberty. This physical and reproductive maturation occurs in an organized pattern, a large part of which is physiologically described and understood (Liew et al. 2017; Martos et al. 2010).

2.1.5 Factors affecting follicle maturation

As people age, there is an unequivocal impact on human reproduction. Socio-economic changes have made it more obvious, because women are waiting to start a family later in life (Carnevale et al. 2008).

Periodic alterations are observed in the woman's ovarian function with age. Women first showed signs of reproductive age when they stopped having monthly menstrual cycles (Astrup et al. 2004).

Older females menstruate on average 29 days each month while younger females menstruate on approximately 28 days each month (Sherman et al. 1976).

During the early follicular phase, FSH hormone levels increase with increasing estradiol levels, but at the same age, levels of LH remain constant (Klein et al. 1996).

Older human female had shorter monthly period due to the shortened follicle stages. Advanced follicular evolution in an older human female is attributed to early recruitment and dominant follicle selection, as a result of the important early rise in FSH hormones level through the latter two weeks of the luteal phase Even though they do not differ considerably, the average pre-ovulation follicle diameter was 19.8 mm in older women while it is about 21.9 in younger human female (Soules et al. 2000).

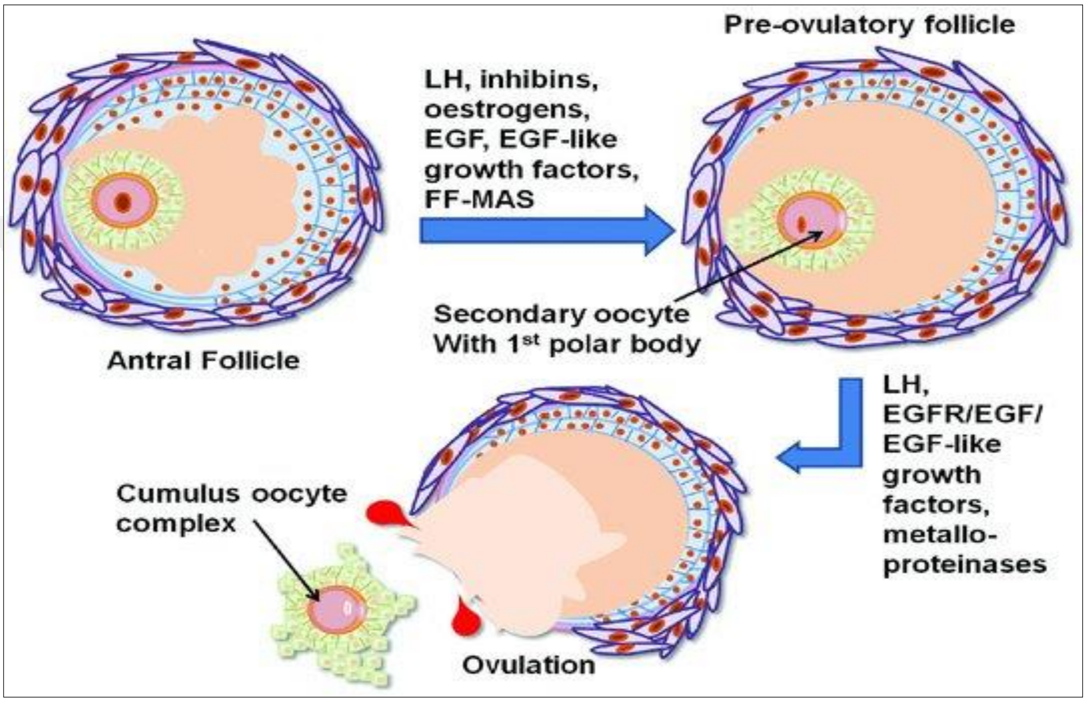

Figure 2.5 Factors affecting follicle maturation

2.1.6 Polycystic ovary syndrome and oocyte developmental competence

The abbreviation (PCOS) refers to polycystic ovary syndrome in women, which is a heterogeneous syndrome. There are many symptoms associated with this syndrome, for example, it is characterized by; androgen excess in the ovaries, hyperinsulinemia from insulin resistance, excessive luteinizing hormone (LH) secretion, polycystic ovaries, and finally decreased fertility (Dumesic et al. 2008).

The developmental competence of oocytes is dependent on alterations in the phenotypic manifestation of reproductive and metabolic disorders in PCOS patients. The oocyte's able to accomplish meiosis and go through embryogenesis and development are what it has to offer for fertility treatments (Heijnen et al. 2006).

PCOS' altered influence on egg implementation is attributable to PCOS' definition, which is simpler than previous definitions. Hyperandrogenism (both primary and secondary) is a clinical diagnosis for PCOS, along with oligomenorrhea (fewer than three periods per month) and polycystic ovaries. The exclusion of all other endocrinopathies, including congenital adrenal hyperplasia (CAH), Cushing's syndrome, androgen-producing tumors, thyroid imbalance, hyperprolactinemia, and the drug-induced androgen increase, serves as the clinical exclusion (Azziz et al. 2006; Rosenfield et al. 2016).

There are a number of possible causes for the association between PCOS and egg development, including (Dumesic et al. 2003): -

- Additionally, research into the capability of oocyte development is hindered by ethical and procedural issues around the use of genuine female eggs and embryos in biomedical research studies.

- Every follicle has its own microenvironment, and it affects ovulation.
- Follicular fluid steroid levels are difficult to control when numerous embryos are simultaneously transported to the uterus via in vitro fertilization, therefore impairing proper embryo implantation.

During the early stages of follicle development, primordial follicles gather into groups and a single individual follicle is chosen to ovulate. It takes around 3 to 6 months for primitive follicle recruitment to Graafian follicle growth (Serafica et al., 2005).

2.2 Polycystic Ovary Syndrome (PCOS)

Increased treatment choices for women with PCOS are made possible by a wider selection of pharmacological formulations and regimens (PCOS). The treatment and management of PCOS is difficult due to the many different challenges that women with this condition must face (Azziz et al. 2006; Zawadzski. 1992).

therapy plans must deal with the three common clinical issues associated with the condition (Asunción et al. 2000): -

- Insulin resistance.
- Menstrual disturbances which related to anovulation.
- Symptoms of hyperandrogenism, such as hirsutism.

Up to 6% of women of childbearing age may be afflicted by PCOS, and it often develops soon after menstruation. It is frequently observed in most women and is connected with insulin resistance which, in many women, results in frequent ovulation. Many practitioners now rely on the NIH's 1990 Compatibility Conference guidelines, but there is significant heterogeneity on the diagnostic criteria (Moghetti et al. 2000).

Hyperandrogenism, anovulatory dysfunction, and the absence of additional reasons are all noted in this group. As a result, PCOS is currently a prediction for exclusion. It is unexpected that PCOS cannot be diagnosed by using ultrasound images of the "polycystic" ovaries. In the case of PCOS, women may not always have to ovulate in order to suffer. PCOS can be diagnosed in women who satisfy the NIH's criteria for PCOS, but those women's ovaries may not appear to have PCOS (Setji et al. 2014).

Polycystic ovary syndrome is often difficult to detect in women with this disease of childbearing age because It has many symptoms thus. The condition causes more than the required amount of male hormones to be produced, resulting in an irregular menstrual cycle. In some cases of PCOS in women, the number of menstruation decreases to only eight cycles per year, or heavy periodic bleeding, because it affects the ovaries that participate in the formation of estrogen and progesterone, which helps to regulate the duration of the menstrual cycle, another symptom is obesity Obese women are more likely to acquire PCOS, while women with PCOS are more likely to be obese. other accompanying symptoms include aHyperandrogenism (hirsutism, acne, alopecia) and excessive anxiety, it has been demonstrated that PCOS may be connected with an increased risk of developing type 2 diabetes (Kitaoka. 1997).

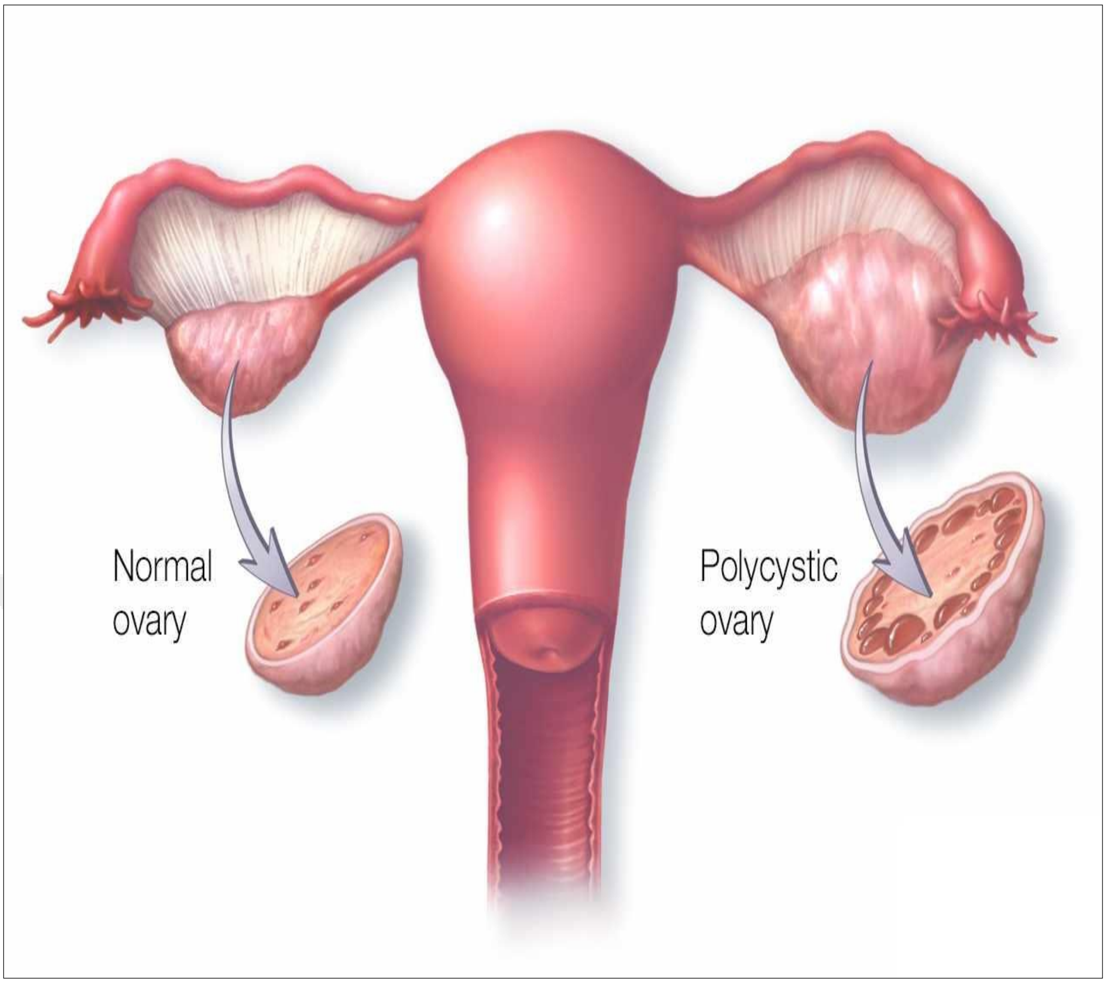

Figure 2.6 Polycystic ovary syndrome (PCOS)

2.2.1 History

Until now, numerous medical societies and workshops have been organizing scientific diagnostic practices with the goal of coming up with a more thorough definition of the illness. laboratory tests as well as results from examinations conducted by the Ophria Institute of the National Institutes of Health, which was based on the analysis of laboratory and clinical data. diagnostic investigations conducted by expert physicians who considered that a woman has PCOS if she exhibits a set of symptoms such as; vitamin deficiency or chronic ovulation, endocrine and related disorders (March et al. 2010).

A number of short- and long-term side effects of PCOS have been described, including a greater risk of difficulties during pregnancy, a worsening chance of conception, as well as tumors. It is difficult to establish the extent of these consequences because of the diverse characteristics of the condition. Also, complicating factors, such as obesity, may be present. Moreover, the phenotypes of PCOS (polycystic ovarian syndrome) vary with each woman's reproductive lifespan; As a result, changes in ovarian function and metabolism control the expression of the disease, and may be implicated in the onset of PCOS in older women and in menopause (Welt et al. 2013).

In women of reproductive age, infertility was one of the primary symptoms of PCOS, according with first description. Following on from the findings of epidemiological studies, it has been concluded that PCOS is the most prevalent cause of an ovulation issue, and that those who ovulate less are more likely to have infertility. 50% of women experienced primary infertility, whereas 25% experienced secondary infertility (Asunción et al. 2000).

2.2.2 Polycystic ovarian morphology

After conducting many investigations and reviewing refer to polycystic ovary syndrome (PCOS) as a standard way to diagnose PCOS (PCOS), Polycystic ovarian syndrome throughout the time of childbearing was discovered to be a factor in PCOS. has important health effects at the present time and also in the long term during the life of the woman. Among these health effects include metabolic disorders and chronic diseases. Polycystic ovary morphology has been considered one of the diagnostic criteria for this syndrome, a general consensus has been reached, and study and cooperation will proceed from there (Kousta et al. 2005).

PCOS causes various long-term health problems for women, for example diabetes, cardiovascular disease, obesity, insulin resistance, lipid disorder, endometrial cancer, high blood pressure and signs of abnormal vascular function. Long-term investigations of women Having defined PCOS must be reached during reproductive age in order to comprehensively comprehend and evaluate the long-term health repercussions. It is essential to identify and choose women with PCOS at that time to establish the timing, manner of treatment, and long-term prevention measures (Kousta et al. & Franks et al. 2007).

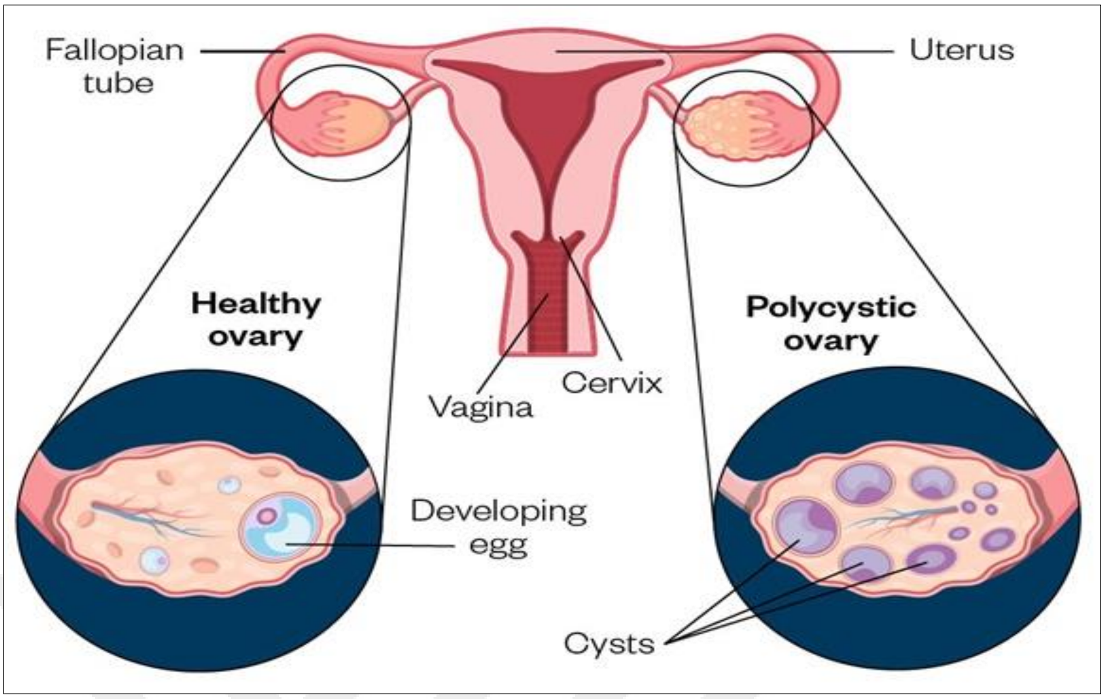

Figure 2.7 Normal ovary compared with a polycystic ovary

2.2.3 Pathophysiology

Since the etiology of PCOS in women of reproductive age is still not fully understood by many physicians and therapists, many of them still consider the issue to be complex and multifactorial (Wallace et al. & Sattar et al. 2007).

Through continuous monitoring of some women with this disease, elevated urinary concentrations and levels of Women with menopause, hirsutism, obesity, and the appearance of polycystic ovaries were shown to have levels of Luteinizing Hormone (LH) and Follicle-Stimulating Hormone (FSH) (Christman et al. 1991).

Once. Later, at the height. In the LH serum concentration relative to the FSH concentration Gonadal dysfunction resulting from hypothalamic-pituitary-pituitary axis dysfunction has been postulated by Yen and colleagues in 1970 (Azziz et al. 2006).

However, there is now consensus on the part of physicians and specialists in this field that the main features of this disease may include several symptoms, for example insulin resistance, abnormal gonadal dynamics, increased androgenicity, On the other hand, it appears doubtful that one single factor is to blame for this mixed up flaw. excess body fat, adrenal gland, pituitary gland, and liver are all implicated, wide range of associated hormonal imbalances (Figure 2.10). leading to disruption of the dominant follicle selection and thus interruption of ovulation (Azziz et al. 2004; Glintborg et al. 2017).

PCOS women with high levels of insulin in their bodies will produce androgens in their ovaries, as well as other hormonal imbalances, such as aberrant follicular development and an inability to menstruate. Abnormalities such as excessive triglycerides, tissue plasminogen activator, and chronic low-grade inflammation can all be consequences of metabolic issues. There is an elevated risk of multiple chronic diseases in patients with PCOS

2.2.4 Thyroid gland

This is a tiny gland, measuring approximately 5 cm, that is located under the skin at the base of the neck, near the Adam's apple. In the center of the gland, the two halves are connected. The thyroid gland is almost always located deep within the neck, making it difficult to palpate and difficult to feel. However, if it is larger, it may be felt, and it may protrude from the base of the Adam's apple or jut out on either side of the trachea. Thyroid hormones have a wide range of effects on the body, including regulating heart rate, increasing metabolism, skin repair, growth, body temperature, fertility, and digestion. TSH is the strongest biomarker of thyroid function (Stathatos 2012).

It has been observed that hypothyroidism can increase the size of the ovaries and work to form some follicles on its wall, similar to what the ovarian cyst produces from incomplete eggs, which impedes the ovaries from performing its function and producing hormones, and leads to menstrual disturbance and infertility (Yamashita et al. 2001).

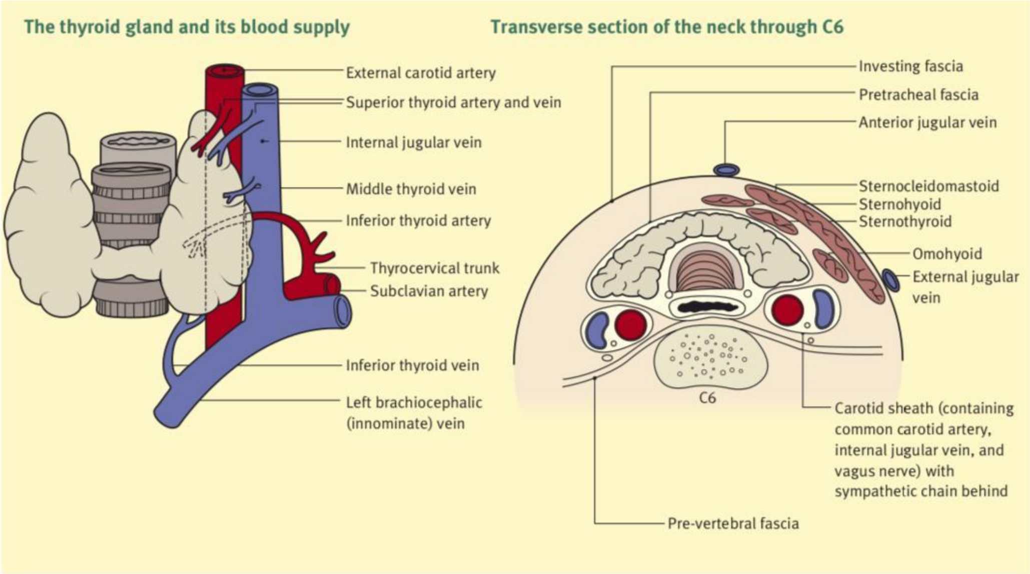

Figure 2.8 The thyroid gland and its blood supply and transverse section of the neck through C6

2.3 Laboratory Evaluation

Laboratory testing is essential for women of childbearing age suspected of having PCOS because It acts as a first line of defense, which keeps out additional viruses. Measurements of some significant hormone such as; In principle, concentrations of these four hormones—luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), and testosterone—could be of significant diagnostic value for knowledge about disease (Sebastian et al. 2018).

However, there are many difficulties in selecting people or performing biochemical tests with adequate diagnostic specificity because the groups of women are heterogeneous. In addition, PCOS treatment might last up to 50 years, during that time several different hormone test protocols alter. Conflicting results about the diagnostic accuracy of the numerous test procedures may be contributed by each of the techniques. Due to the new diagnostics becoming more available, several hormone testing provide a more specific result for this illness (Amiri et al. 2014).

Below, the advantages and disadvantages of the regularly used hormone measurements used to support the diagnosis of PCOS are outlined.

2.3.1 Luteinizing hormone (LH)

Glycoprotein hormones (such as FSH, thyroid-stimulating hormone (TSH), and human chorionic gonadotropin (hCG)) belong to the glycoprotein hormone family, which also includes luteinizing hormone (LH). These hormones have particular biological characteristics. An elevated LH level is hypothesized to contribute to ovulation and polycystic ovary syndrome (PCOS) in women, which means a higher likelihood of ovarian androgen production and hence an increased chance of getting pregnant (Themmen 2005), see Figure 2.8.

One of the typical biological symptoms of PCOS in women of childbearing age is an elevated level of circulating LH, which is thought to be related to gonadotropins in the pituitary gland. Through many investigations, it has not been proven that LH hormone contributes to events that occur before ovulation (Liu et al. 2012), see Figure 2.9.

It can be concluded depending on some previous investigations that LH contributes to folliculogenesis through analysis of gonadotrophin levels in the blood and success rates after induction of follicular maturation with external gonadotropin (Humaidan et al. 2004).

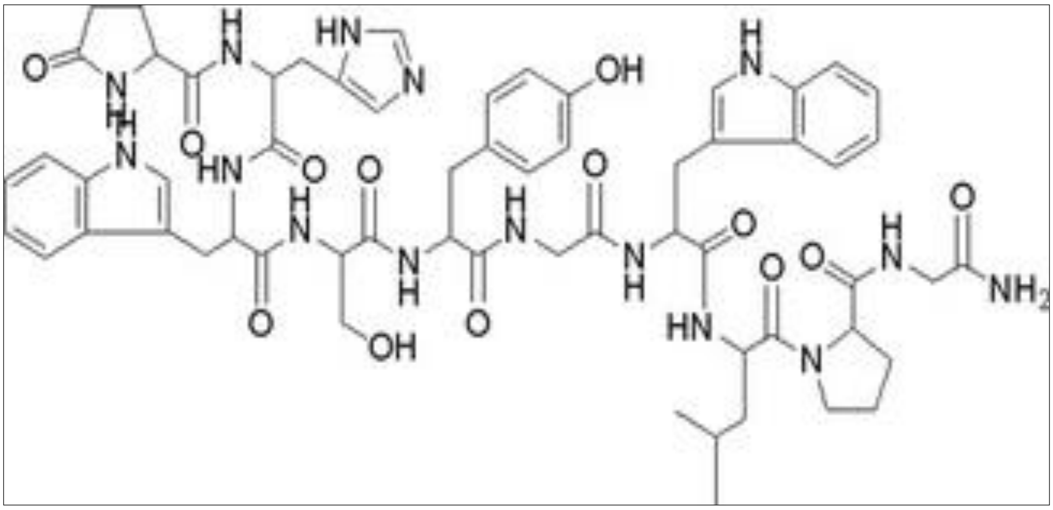

Figure 2.9 The structure of luteinizing hormone (LH)

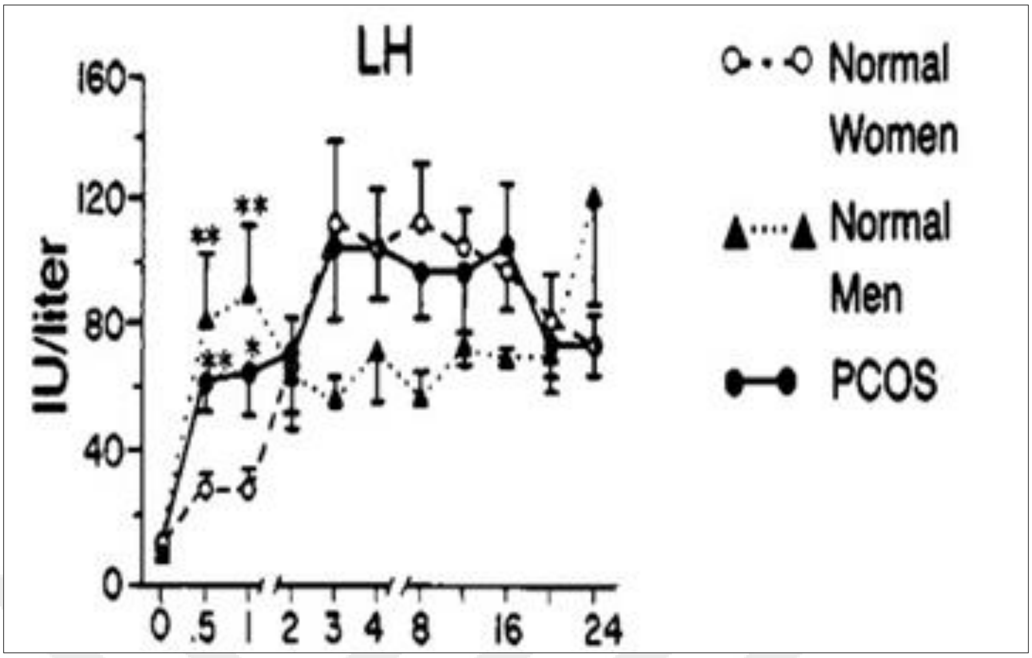

Figure 2.10 The structure of LH hormone

2.3.2 Follicle stimulating hormone (FSH)

FSH is a protein hormone involved in reproduction. FSH determines many important matters such as reproductive physiology, fertility regulation, diagnosis and treatment of reproductive disorders. FSH has many molecular forms in both the incorporation of organ processes, together with various types of screening There are a variety of types of FSH, which change based on the nature of the illness (Lunenfeld and Lunenfeld 1997), see Figure 2.10.

FSH criteria are considered by WHO from various sources as being the main sources for diagnosis and treatment. The biological techniques and therapeutic products used in these international standards are nearly identical to each other and with the medications described in human bioassay (Barad et al. 2009).

Gonadotropin inappropriately released is a symptom that is not currently incorporated into the diagnostic criteria for PCOS and using aberrant gonadal secretion patterns for educational purposes, PCOS has been shown in women of childbearing age to have many symptoms, such as: Luteinizing hormone (LH) levels are higher, whereas follicle-stimulating hormone (FSH) levels are lower. The majority of women with PCOS suffer from amenorrhea, meaning they do not menstruate (Chun 2014). As can be seen in the figure 2.11.

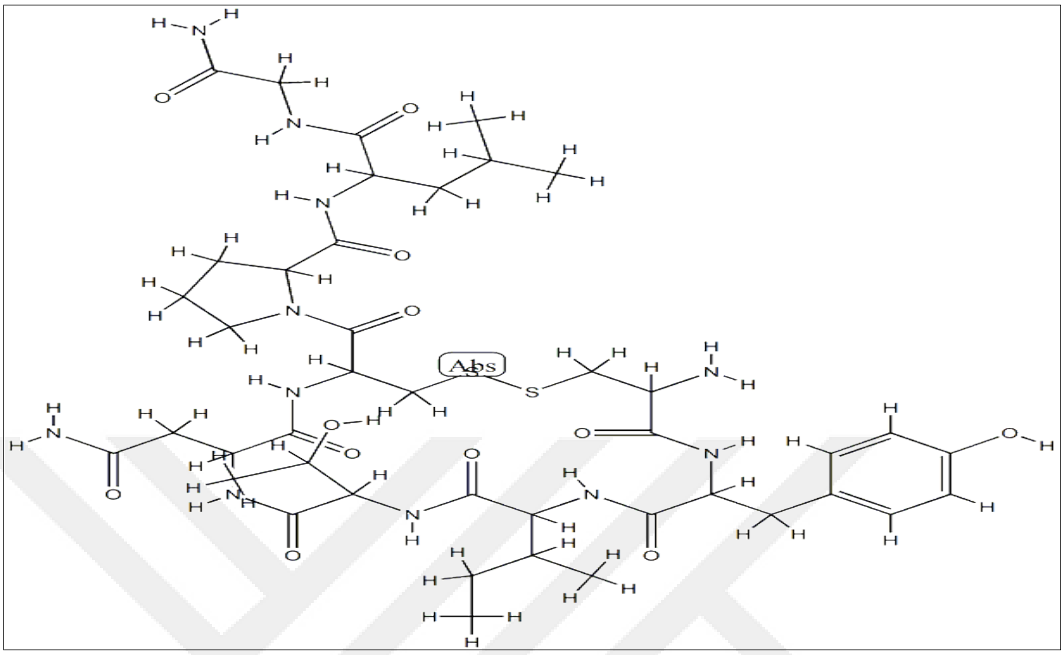

Figure 2.11 The structure of the follicle stimulating hormone (FSH)

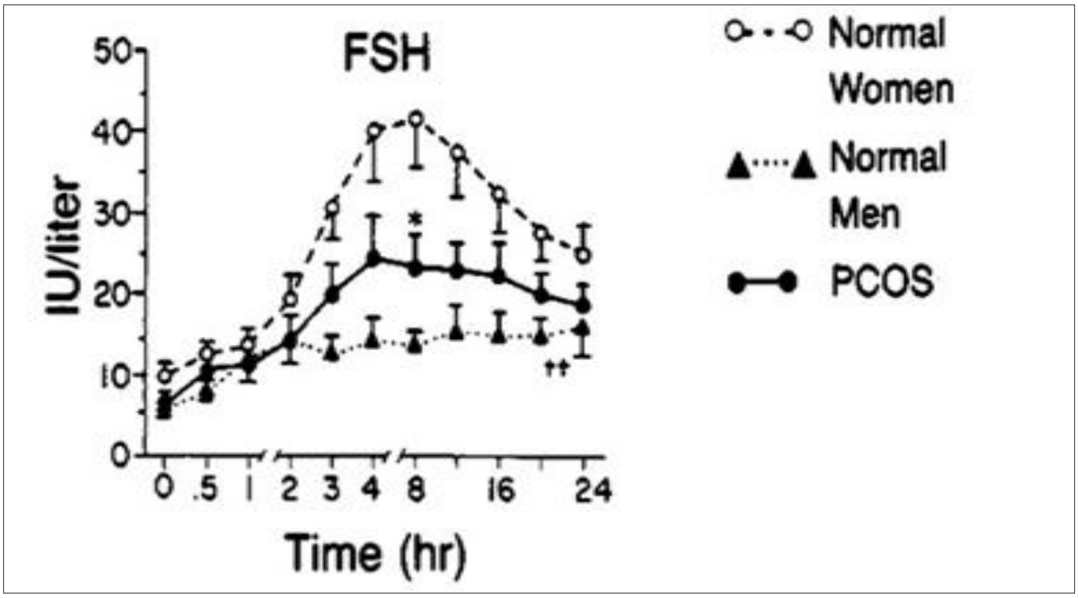

Figure 2.12 The structure of the FSH hormone

2.3.3 Thyroid-stimulating hormone (TSH)

In order to compare the routine laboratory values of women with PCOS to the levels of TSH, an investigator conducted a research, clinical and hormonal characteristics, as well as metabolic indicators, did not exhibit any variations. Thus, the current data do not justify changing the diagnostic or therapeutic therapy for women with PCOS when TSH levels are normal (Benetti-Pinto et al. 2017).

A comparison of multiple TSH levels, using the same measurements, showed that total cholesterol and triglyceride levels varied. In women with PCOS and normal thyroid function, no significant differences were detected in other human and normative parameters or in the majority of laboratory values (Ganie et al. 2011).

2.3.4 Testosterones

An investigator found that women with PCOS in their 40s and around the expected life span had high testosterone levels. while the link between these age-related events remains unproven, the scientist said that this rising trend in PCOS among women is associated with the regularity of their menstrual cycles as they age (Dahlgren et al. 1992).

To confirm or verify the findings of the investigator, the researcher took random blood samples throughout the menstrual cycle, and found that the women who were in the middle third of the cycle had higher testosterone levels (Judd et al. 1973).

To date, there is no established explanation for why women with PCOS show a rise in testosterone concentrations with age. It is assumed that in PCOS, LH and insulin are two of the key drivers of testosterone production. The lower testosterone levels seen in women with PCOS were not likely due to changes in LH levels, as the women with PCOS had greater LH levels (Winters et al. 2000).

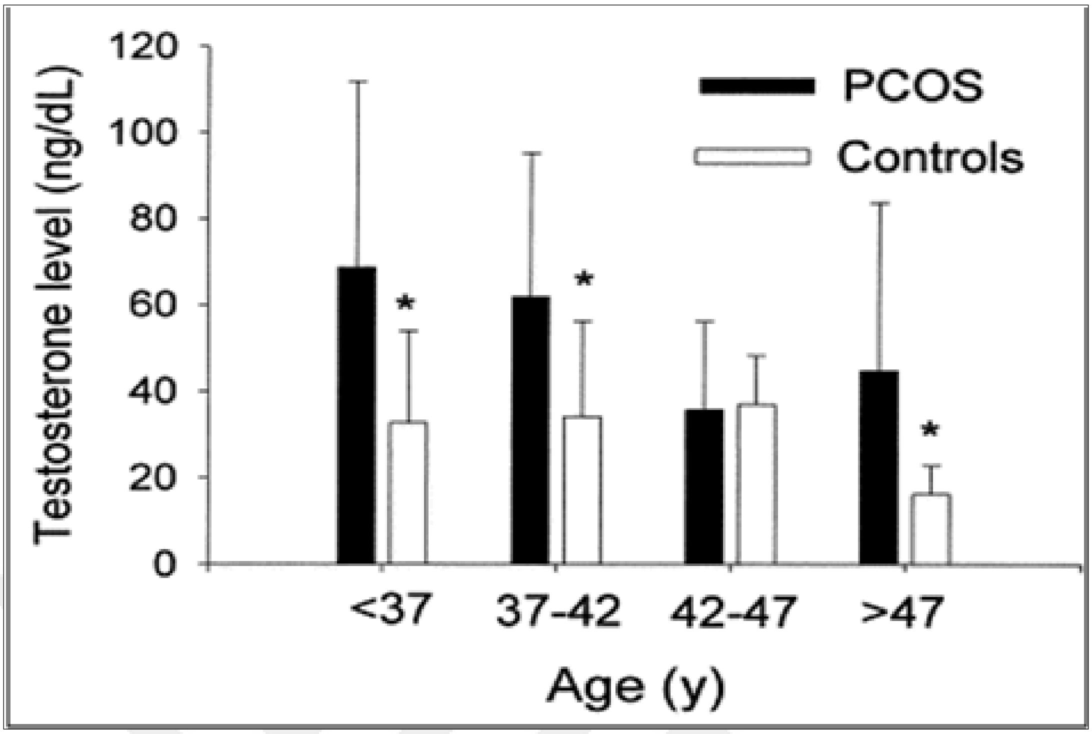

Figure 2.13 Serum testosterone levels increase in middle age in women with polycystic ovary syndrome as a function of age

2.3.5 Relation between (LH/FSH)

The study of the relationship between (LH/FSH) is important in many aspects, as an increase in FSH concentrations, without accompanying changes in LH concentrations, indicates reproductive aging in women. FSH hormone-modifying, including estradiol, epinephrine, activing, and follistatin, are known as hormonal alterations. It is possible that an elevated concentration of FSH could promote an accelerated depletion of the primordial follicle supply (Soules et al. 2000).

Women of normal childbearing age emit the same hormone - luteinizing hormone (LH) - and the same amount of the second hormone - follicle stimulating hormone (FSH) - at nearly the same time. The ratio of FSH to LH is (in a ratio of 1:1). When a woman has polycystic ovaries, the ratio of elimination is one-to-two. The LH-FSH hypothalamic polypeptide regulates reproductive activities by secreting from the hypothalamus. of gonadotropins from the anterior pituitary gland (Lewandowski et al. 2011). See Figure 2.13.

There are various reasons for this, for example: low levels of serotonin and dopamine, elevated levels of insulin, and caloric restriction in the short term. It is the rapid secretion of GnRH that can lead to high levels of LH, so adjusting the diet and lifestyle can lead to an increase in the release of GnRH and a decline in luteinizing hormone results in decreased progesterone secretion, which causes PCOS symptoms to get worse (da Silva Feuser et al. 2014).

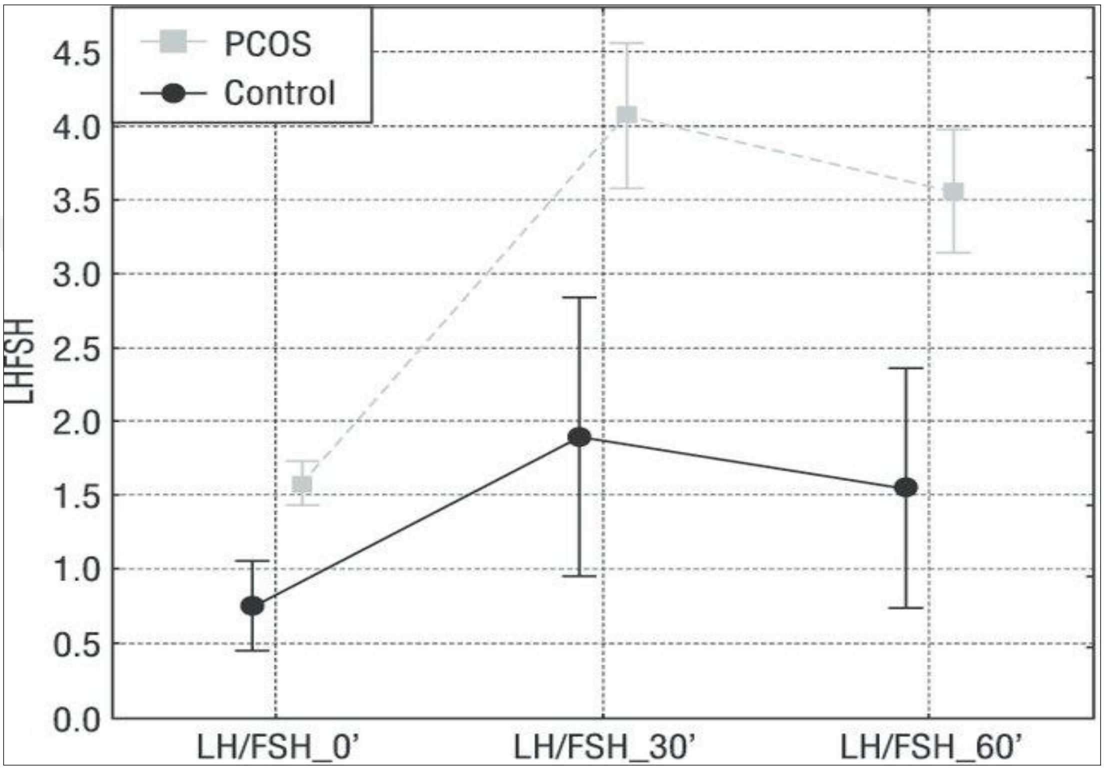

Figure 2.14 The ratio of LH/FSH in PCOS

3. MATERIALS AND METHODS

3.1 Materials

3.1.1 Syringe

A syringe is a medical device, its configuration is similar to a pump, consisting of a tapered tube at one end, and a piston or cylindrical arm passes inside it, and both the piston and the arm work to suction, push or withdraw liquids.

3.1.2 Tourniquet

It is a tool that used to pressurize the vein to facilitate the process of blood drawing by Syringe from the selected person for both the Patient Group and Control Group.

3.1.3 Tube EDTA

Ethylene tetra-acetic acid (EDTA) is a chemical compound of the polyamino carboxylic acid class, and the conjugate base is called ethylene diaminetetra acetate. EDTA is a water-soluble and colorless solid that is used for all tests that require a whole blood.

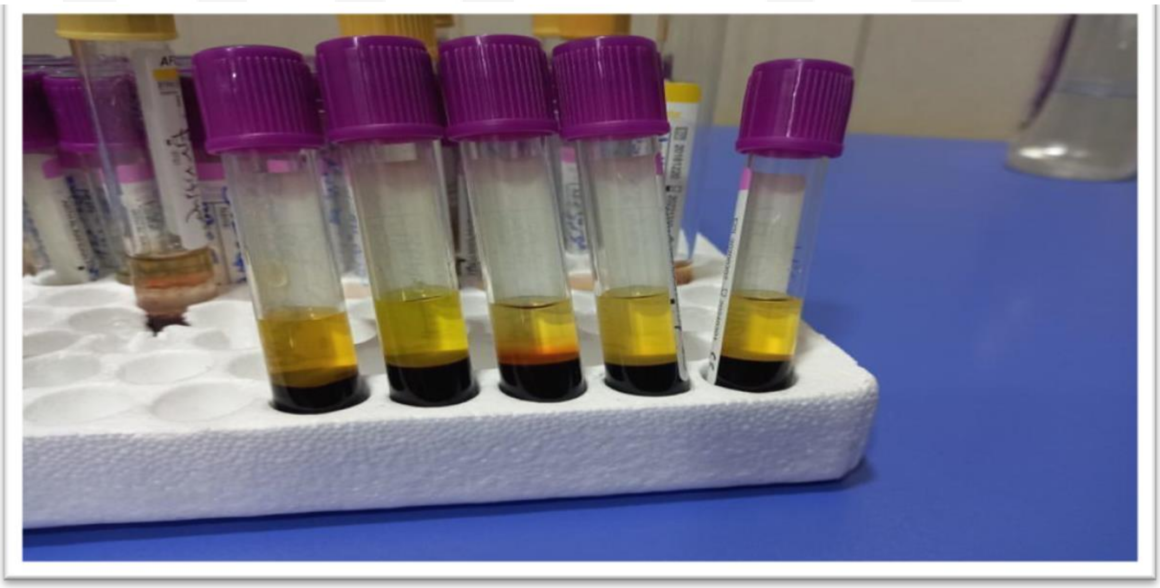

Figure 3.1 Tube EDTA

3.1.4 Centrifuge

A centrifuge is a device that is usually driven using an electric motor, some older models are hand-operated that rotates an object placed inside it around a fixed axis. The idea of operation depends on the principle of sedimentation. And its goal is to separate particles or material according to the difference on their density.

Figure 3.2 The centrifuge device

3.1.5 Pipet

It is a medical laboratory tool that is used to transfer or measure the volume of a liquid. This tool is available in several shapes and volume. It can also be made from several materials; it may be transparent or opaque.

Figure 3.3 Pipet

3.1.6 Dropper

It is one of the medical laboratory instruments, it uses to measure and convey the selected liquid.

3.1.7 Hitach

It is one of the types of small tubules that uses in the medical experimental analysis.

3.1.8 Kit

In this study, four different types of kits were used, as shown (TSH, LH, FSH, TESTO).

Figure 3.4 Kits

3.1.9 Cobas E411

It is the hormone analysis device that was chosen in this study.

Figure 3.5 Cobas E411

3.1.10 Cotton and some sterilizers

3.1.11 Chlorine

It is a sterile material used for sterilization that kills bacteria and viruses effectively

3.2 Methods

3.2.1 E411 Cobas (Immunoassay System Routine Operation)

Immunoassay technique for analysis. Quantitative and qualitative in vitro assay determinations are supported by the product. Analyzer samples can be handled in either a rack or disk sampling setup.

Subject	**Cobas E411 Immunoassay System Routine Operation**
Index Number	**Lab-1599**
Section	**Laboratory**
Subsection	**Regional/Affiliates**
Category	**Departmental**
Contact	**Rachel Blum**
Last Revised	**8/8/2019**
Part NO	**741-0500**
Serial NO	**1 8 P 8 - 0 2**
Supply Voltage	**AC100-240V**
Frequency	**50/60HZ**
Power Consumption	**1000VA**

This is a fully automated, random access, software-controlled system for immunoassay analysis. There still are three sets of tests you can do on the system: competitive principle for analyses which are molecularly tiny, for bigger investigations, the sandwich principle is appropriate, whereas for detecting antibodies in the sample, the bridging principle should be used.

For an ECL process, the surface of the electrode must generate highly reactive species from safe precursors. The reactivity of this family of molecules leads it to emit light.

A company's guiding principles include: -

Before starting maintenance procedures in the morning, turn the front switch on the analyzer to the OFF position.

1. Inspect the condensation within the reagent compartment by removing the reagent compartment cover and the reagent wheel. Completely wipe away any wetness. to replace the wheel or the lid

2. Clean the S/R probe with filtered water on gauze, and then remove the water via wiping. 70% Isopropanol should be used if the probe looks dusty.

Figure 3.6 Preparation immunoassay system routine operation before using

After completing the operation of the device and placing the kits in its Disk (position) The device scans to find out the type of reagent and its location in the disk

The calibration and control are made for the new reagents used (LH, FSH, TSH.TESTO) Calibration It is a group of measurement operations that are carried out under specific conditions using measuring devices and tools based on national or international standards that achieve the units of the International System of Measurement (SI). These processes determine the accuracy of the measuring devices and their suitability for the purpose for which they are used and the extent of their conformity with the international system of measurement in accordance with international standards.

And each reagent has a calibration and control (vails) a specific it but they all work on the same mechanism after completing the calibration and the appearance of its curve a making sure of its accuracy after that Control must be done.

Three types of control are made of normal and abnormal high (above the normal range level of the test being examined) and unnatural and low (below the normal range level of the test being examined). The goal of them (calibration and control) to identify Reagent works well and gives correct results or not.

Figure 3.7 Vials control and calibration

At first, the site of blood extraction (the patient's hand) is sterilized by a special sterilizer, then a tourniquet is placed, then the blood sample is drawn by (a syringe) from the vein of the patient's hand, and then a tube is taken and blood is placed in it. Then the tube is placed into the centrifuge for separation.

After the completion of the calibration and control, the plasma sample is placed in its place, and the device scans to find the position of the tube and to know the type of analysis required, then the probe takes (draws) a quantity of plasma (sample) size 10 to 50 μl for each test).

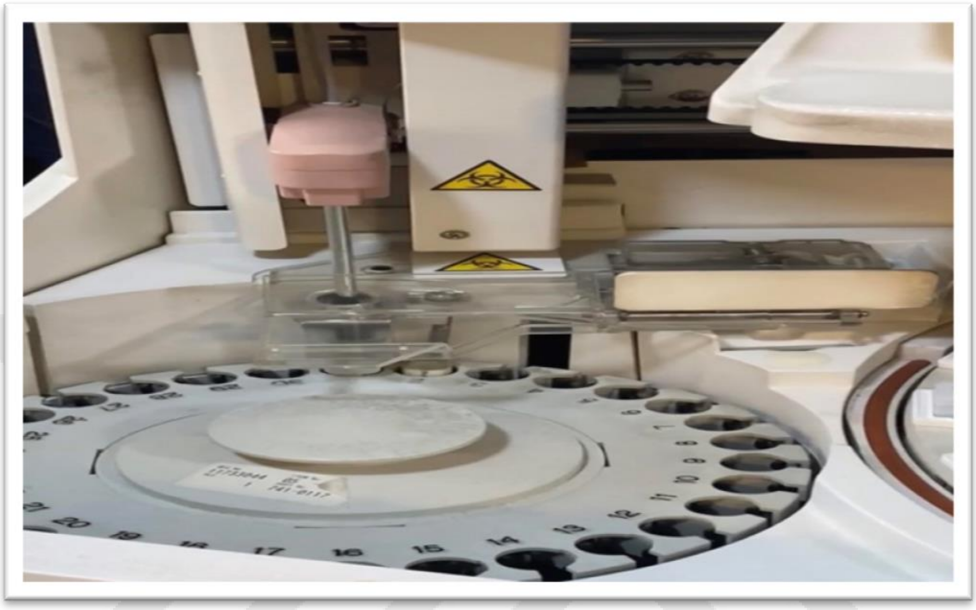

Figure 3.8 A probe drawing from the sample

Then the other probe takes (withdraws) a quantity of the reagent as it is in the figure3.9

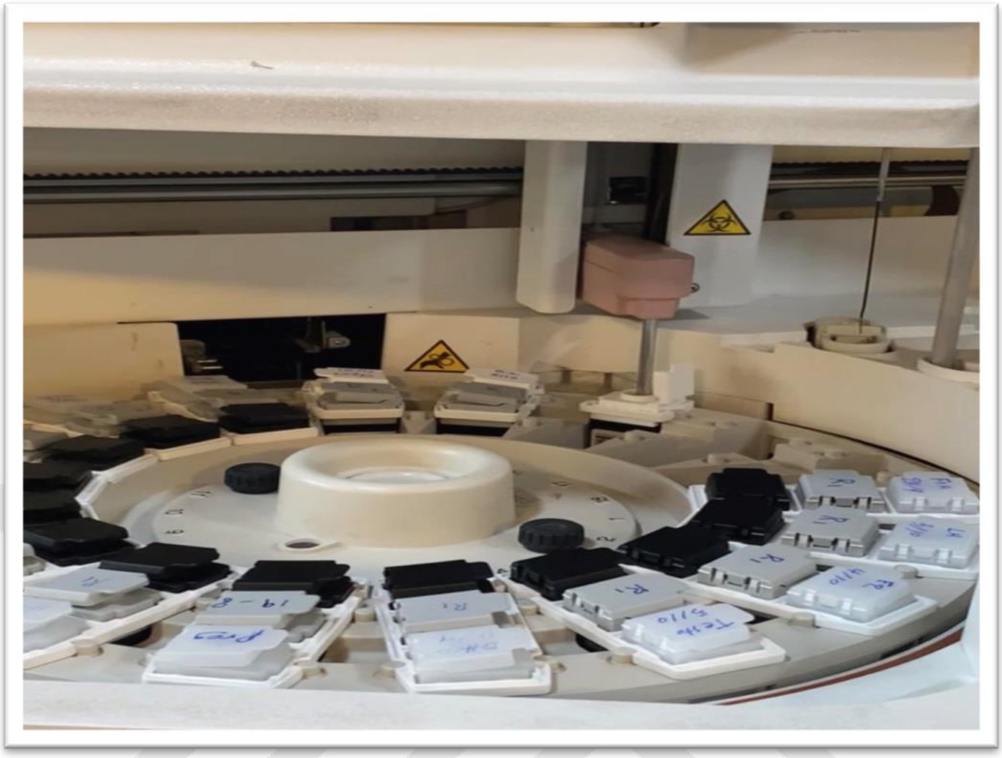

Figure 3.9 A probe drawing from the reagent

The reaction takes place after that and the result is obtained for a period ranging from 9 minutes to 20 minutes, depending on the quality of the analysis due to the method of measurement that is ECL. Another advantage of the device is the possibility of adding other samples at any point in the process.

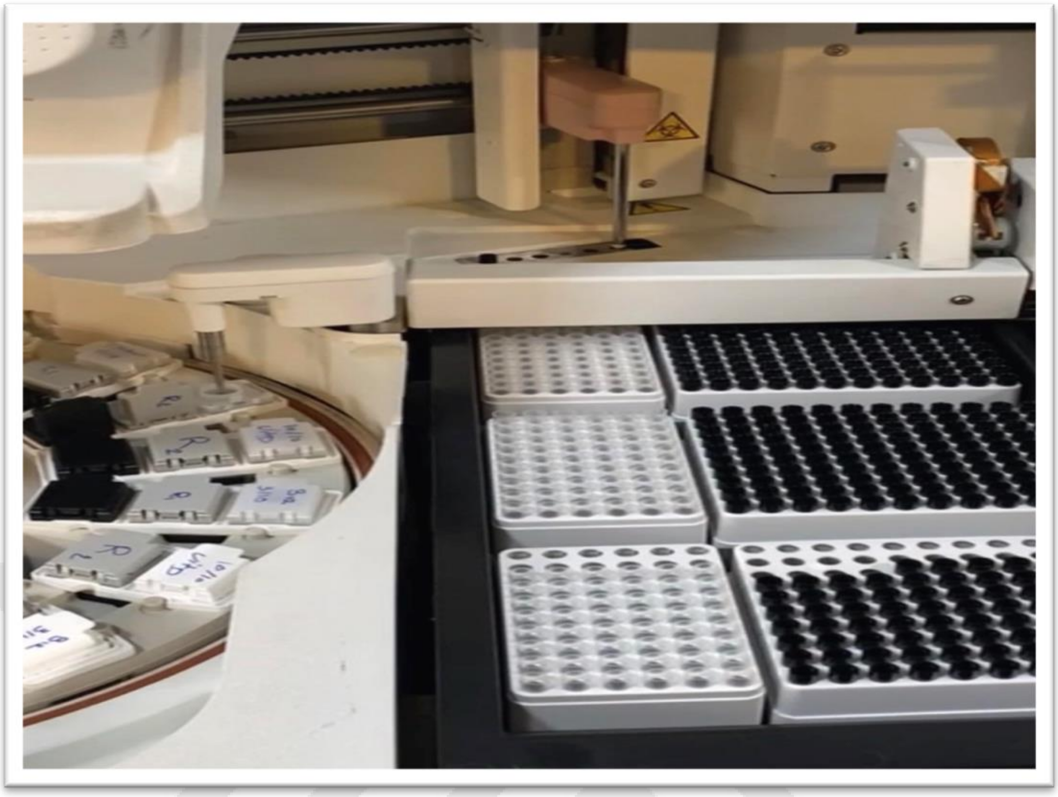

Figure 3.10 Explanation of the probe working

4. RESULTS AND DISCUSSION

4.1 PCOS and Thyroid Diseases

The most commonly endocrine issue seen in women of reproductive age is polycystic ovary syndrome PCOS has been found to be connected with specific metabolic and cardiovascular disease, as well as with immunological diseases, predominantly autoimmune thyroid disease (Romitti et al. 2018). This study included 135 persons, their ages between 26- 66 year for analysis. Control group 45 healthy subjects (Group A), while Group B involved 45 patients with PCOs and, Group C including 45 Patients with PCOs and thyroid disease.

4.1.1 Age with PCOs

The findings of this research were that have been showed that no significantly between the mean age of the Control group (A= 25.4 ± 7.73) and two patients groups (B= 27.2 ± 6.62; C= 26.7 ± 6.42 year) respectively, in same time, as shown in Table 4.1 and Figure 4.1.

Table 4.1 Age (year) for patients and control group

Variable	Groups	Mean ± SD	Sig.
	A	25.4 ± 7.73	0.548
	B	27.2 ± 6.62	0.548
	C	26.7 ± 6.42	0.548
	Total	26.4 ± 6.94	0.548
P > 0.05 = Mean considerable variance between Groups. P < 0.05 = Mean non- considerable variance between Groups.			

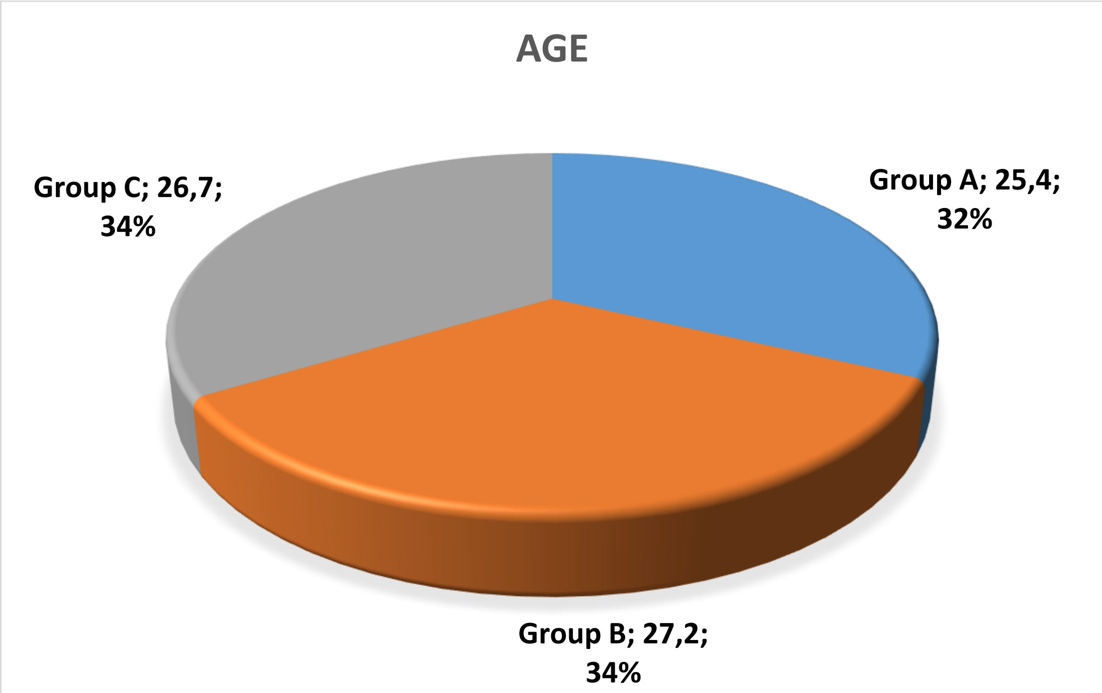

Figure 4.1 The mean average age of the three groups (A, B, C)

4.1.2 LH and FSH with PCOs

Also the mean of LH (IU/l) was has a significant difference between patient's groups (B= 16.8 ± 11.5; C= 18.7 ± 14.5) when compared to controls group (5.90 ± 2.73) in women patients with PCOS. It can be seen the difference between groups as shown in Table 4.2 and Figure 4.2.

Table 4.2 The average of LH (IU/l) levels in the three groups (A, B, C)

Variable	Groups	Mean ± SD	Sig.
	A	5.90 ± 2.73	0.001
	B	16.8 ± 11.5	0.001
	C	18.7 ± 14.5	0.001
	Total	13.8 ± 12.2	0.001
P> 0.05 = Mean considerable variance between Groups.			
P< 0.05 = Mean non-significant difference between Groups.			

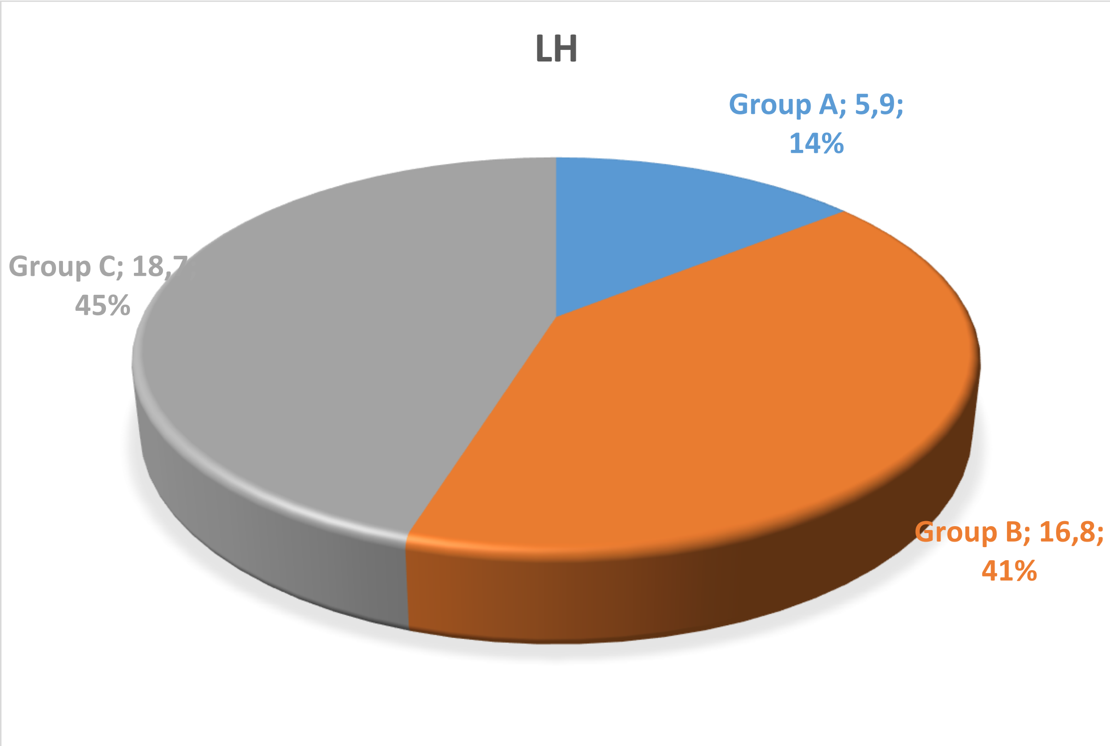

Figure 4.2 The average of LH (IU/l) levels in three groups (A, B, C)

Table 4.3 The average of FSH (IU/l) levels in three groups (A, B, C)

Variable	Groups	Mean ± SD	Sig.
	A	6.36 ± 2.04	0.07
	B	5..27 ± 3.87	0.07
	C	5.92 ± 4.71	0.07
	Total	5.85 ± 3.71	0.07
P > 0.05 = Mean considerable difference between Groups.			
P < 0.05 = Mean non-significant difference between Groups.			

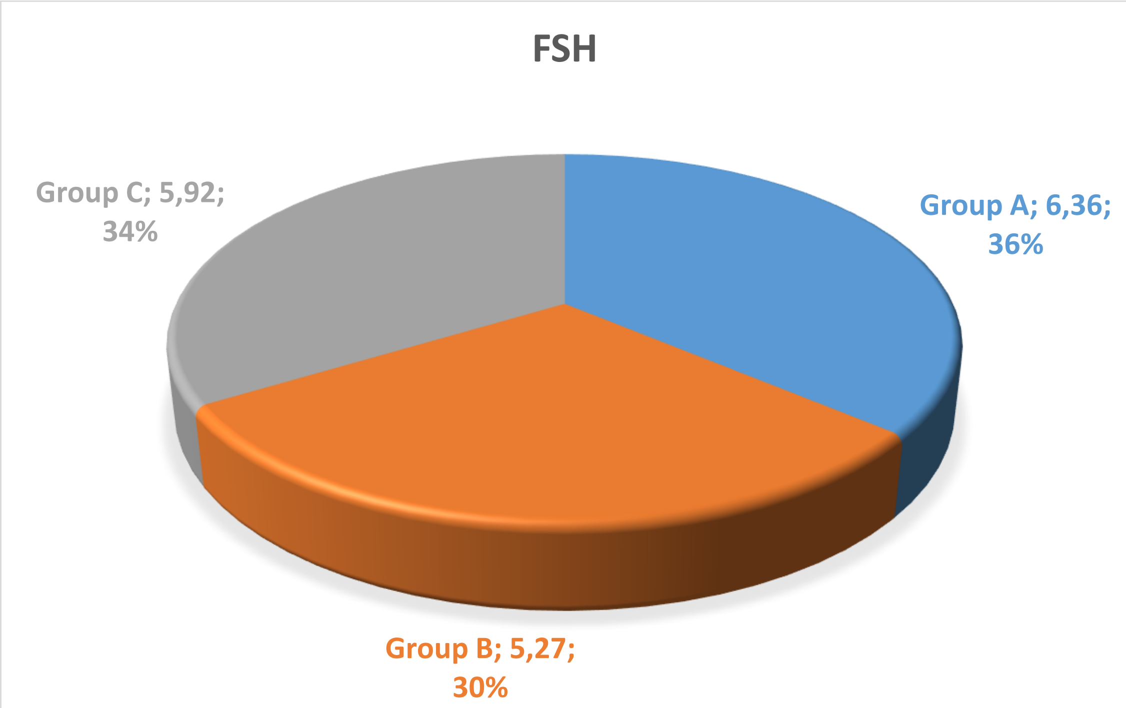

Figure 4.3 The average FSH (IU/l) levels in three groups (A, B, C)

4.1.3 Testosterone and TSH with PCOs

The mean of TSH (µIU/mL) was has a significant difference between patient's groups (C= 5.99 ± 1.02) and wasn't has a significant difference between patient's groups (B= 2.26 ± 1.07) when compared to controls (2.13 ± 0.87) group in women patients with PCOS. It can be seen the difference between groups as shown in Table 4.4 and Figure 4.4.

Table 4.4 The average of TSH (µIU/mL) levels in three groups (A, B, C)

Variable	Groups	Mean ± SD	Sig.
TSH (µIU/mL)	A	2.13 ± 0.87	0.26
	B	2.26 ± 1.07	0.26
	C	5.99 ± 1.02	0.26
	Total	3.46 ± 2.05	0.26
P> 0.05 = Mean considerable difference between Groups.			
P< 0.05 = Mean non-significant difference between Groups.			

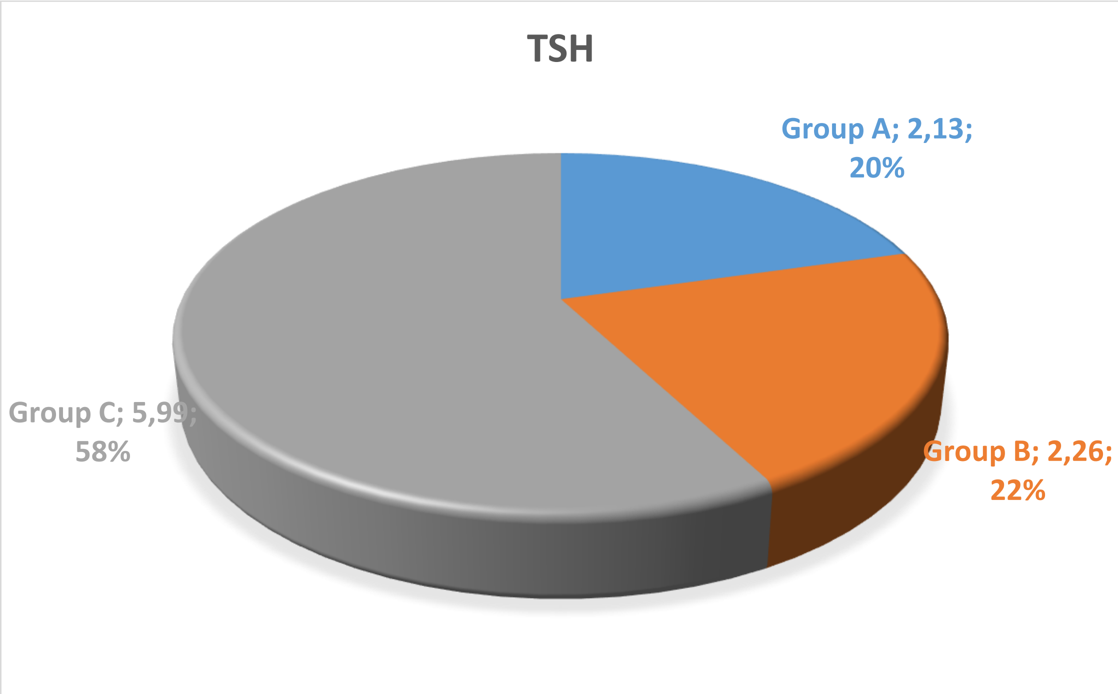

Figure 4.4 The average of TSH (µIU/mL) levels in three groups (A, B, C)

Also in this study, the mean average of testosterone level (ng/mL) was has a significant difference between patient's groups (B= 0.90 ± 0.63; C= 1.12 ± 0.86) when compared to controls Group (0.22 ± 0.09) in women patients with PCOS. It can be seen the difference between groups as shown in Table 4.5 and Figure 4.5.

Table 4.5 The average testosterone (ng/mL) levels in three groups (A, B, C)

Variable	Groups	Mean ± SD	Sig.
Testostrone (ng/mL)	A	0.22 ± 0.09	0.001
	B	0.90 ± 0.63	0.001
	C	1.12 ± 0.86	0.001
	Total	0.75 ± 0.72	0.001
P> 0.05 = Mean considerable difference between Groups. **P< 0.05 = Mean non-significant difference between Groups.**			

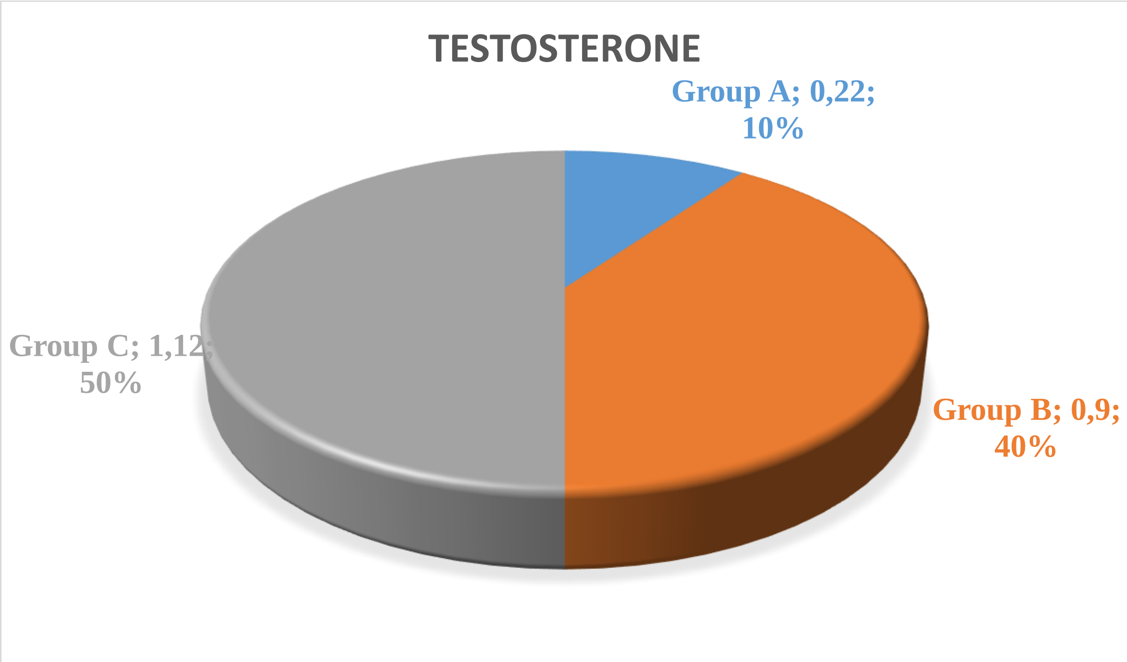

Figure 4.5 The average testosterone (ng/mL) levels in three groups (A, B, C)

4.1.4 LH/FSH Ratio with PCOs

From anther hand, the mean of LH/FSH (%) was has a significant difference between patients groups (C= 3.25 ± 0.59; B= 3.20 ± 1.07) when compared to controls (0.98 ± 0.41) group in women patients with PCOS. It can be seen the difference between groups as shown in Table 4.6 and Figure 4.6.

Table 4.6 The average ratio of LH/FSH levels for patients and control group

Variable	Groups	Mean ± SD	Sig.
	A	0.98 ± 0.41	0.01
	B	3.25 ± 0.59	0.01
	C	3.20 ± 1.07	0.01
	Total	2.48 ± 1.29	0.01
P> 0.05 = Mean considerable difference between Groups.			
P< 0.05 = Mean non-significant difference between Groups.			

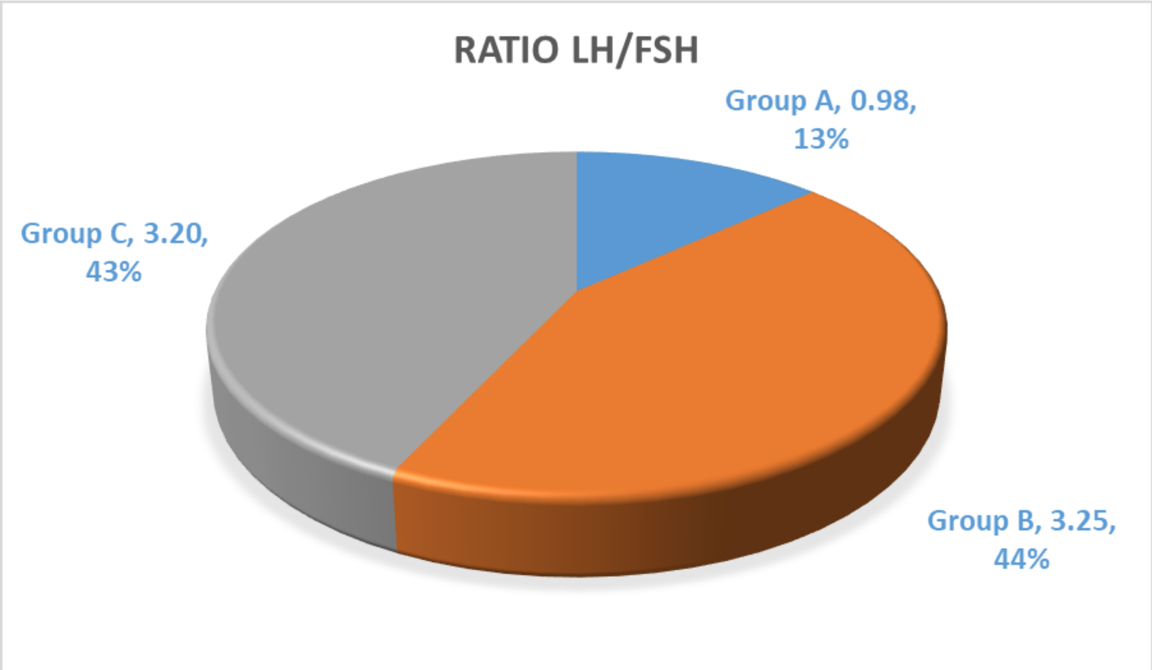

Figure 4.6 The average ratio of LH/FSH levels in three groups (A, B, C)

5. CONCLUSIONS AND RECOMMENDATIONS

5.1 Conclusions

For the individuals with polycystic ovarian syndrome, three different groups were compared to a control group in this study. There were no significant differences between the age expressions of patients (Group B) and the control group (Group A). As a woman ages, the ovaries release less androgens, and the adrenal glands generate less with time. With age, both the number of ovarian follicles and the volume of each follicle decrease. It appears that the rate of decline in follicle number is greater than that of ovarian volume. The observed incidence and polycystic ovarian syndrome could be affected by these age-related changes (Hsu 2013), The results of this investigation are due to fact. Pregnancy problems in polycystic ovarian syndrome patients are rare when the difference in age and weight between these patients and controls is kept to a minimum (Haakova et al. 2003). Also, this study has been shown to be consistent with other research.

For this study, the mean levels of LH and FSH were both significantly higher in patients with PCOs, compared to control subjects. LH levels were greater in women with PCOS at baseline and when stimulated (9.09 ± 5.56 vs 4.83 ± 1.71 IU/L, 35.48 ± 31.4 vs 16.30 ± 6.68 IU/L, 33.86 ± 31.8 vs 13.45 ± 5.2 IU/L, at 0, 30 and 60 mins post GnRH, respectively, $p < 0.0001$). The baseline and stimulated FSH concentrations were the same amongst the groups (Lewandowski et al. 2011), This investigation confirmed our findings.

An abnormal LH/FSH ratio of more than 2 was acceptable. It was discovered that 65 women had normal gonadotropin levels (55 percent; group 2). The ratio of LH to FSH showed substantial differences between normal and high normal values (Banaszewska et al. 2003), This research agrees with our research. Both groups showed similar increases in the amount of LH or FSH when compared to their respective baseline values (Lewandowski et al., 2011), also, this study an agreed with our study.

Women with polycystic ovarian syndrome had higher testosterone than the women that did not have PCOS. ($p = 0.0002$), androstendione ($p = 0.0021$), 17OH-progesterone ($p < 0.0001$) also had increased numbers of insulin resistance.at least one [source of an] increased concentration only androgens were identified, although 58.1% of women with polycystic ovary syndrome (Lewandowski et al. 2011), this study an agreed with our study.

5.2 Recommendations

The study identified in the laboratory research on PCOS and thyroid diseases, and recommended what should be studied to provide information in the following areas: As samples are from an overcrowded Populated area, we recommend increasing samples Work in central laboratories for the purpose of increasing the number of analyzes or tests for the patient.

Make a medical history for the patient to see previous examinations and results, the limited collection of the study sample from one region, and accordingly, more detailed research must be done in the future.

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