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A Comparison of Color Doppler Sonography Findings in Polycystic Ovarian Syndrome Patients and Healthy Women

A scientific dissertation Submitted to the College of Medicine-Diyala University in partial fulfillment of the requirement of M.B.Ch.B

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بِسْمِ اللَّـهِ الرَّحْمَـٰنِ الرَّحِيمِ

(يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ وَاللَّهُ بِمَا تَعْمَلُونَ خَبِيرٌ)

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ABSTRACT

Background And Objective: **Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder in reproductive-age women. The assessment of uterine and ovarian artery resistance indices (RI) can provide additional information on pathophysiology of the syndrome, and can be applied as a diagnosis criterion in suspected cases of PCOS.**

This study aims to compare the parameters of uterine artery blood flow and ovarian stromal artery in PCOS patients and healthy women.

Method: **This cross-sectional study was performed on 20 women with PCOS (PCOS group) and 20 healthy women (control group). In the initial evaluations, age, body mass index, levels of follicle stimulating and luteinizing hormones, as well as severity of hirsutism and acne were recorded. Then, ovarian volume, uterine and ovarian artery RI and the rate of vascularization of ovarian stromal arteries were measured and compared with each other using Gray-scale and color Doppler sonography (CDS).**

Conclusion: **According to the CDS findings, ovarian stromal and uterine blood flow parameters were significantly different in the PCOS and control groups.**

Results: **Results of present study showed there is significant difference ($p<0.05$) between BMI, FSH, LH markers and study groups. Mean levels of BMI, FSH, LH markers were high in PCOS than control. In contrast, it's showed there is no significant different ($p>0.05$) between age and study groups. And showed there is significant difference ($p<0.05$) between Right Ovarian Volume (ml), Left Ovarian Volume (ml), Right Ovarian Artery RI, left ovarian artery RI, Left Uterine Artery RI, Right Uterine Artery RI markers and study groups.**

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1. Introduction

1.1: The ovaries (TA: ovarium [1]) are paired female gonads of the reproductive and endocrine systems. They lie within the ovarian fossa on the posterior wall of the true pelvis and form part of the adnexa.

Gross anatomy

The ovaries are firm and ovoid in shape and measure approximately 1.5-3.0 cm × 1.5-3.0 cm × 1.0-2.0 cm (length x width x thickness) (corresponding to a volume of 1.2-9.4 cm^3). An ovary typically weighs 2-8 g, they change during life and double in size in pregnancy.

Typically they lie on the peritoneum of the pelvic wall in a shallow fossa in the angle between internal and external iliac vessels on the obturator nerve but have variable location secondary to their mobility. They are oriented with their long axis oblique, with lateral and medial surfaces, uterine and tubal ends, and mesovarian and free borders.

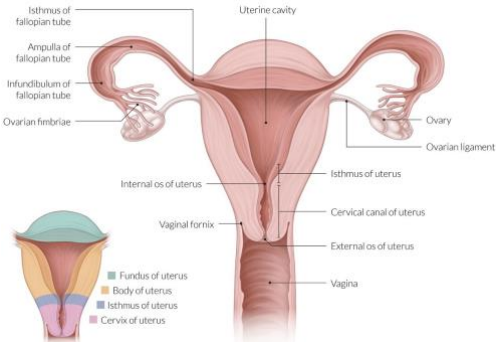
The suspensory ligament of the ovary, a peritoneal fold, runs from the sidewall of the pelvis to the ovary. The ovarian vessels run in this ligament, crossing over the external iliac vessels.

Each ovary is attached to the posterior lamina of the broad ligament by the mesovarium, which is continuous with its outer coat. A third attachment, the ovarian ligament, is a continuation of the round ligament and attaches the ovary to the side of the uterus.

Despite all its attachments, the ovary is very mobile, especially in women who have had children. It is frequently found behind the uterus in the pouch of Douglas. [2]

Relations

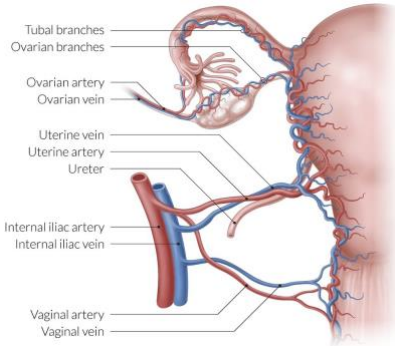
- anteriorly: broad ligament, mesovarium, obliterated umbilical artery
- posteriorly: ureter, internal iliac vessels, suspensory ligament with ovarian vessels
- superiorly: external iliac vessels
- inferiorly: levator ani
- medially: ovarian ligament attaching ovaries to uterus, pararectal fossa and rectouterine pouch, bowel loops
- laterally: obturator vessels and nerves in ovarian fossa, obturator internus and fascia, parietal peritoneum of pelvic wall. [3,4]



Arterial supply

The primary blood supply to the ovary is the ovarian artery, although there is some anastomosis with branches of the uterine artery

- ovarian artery
- ovarian branches from the uterine artery [7]



Venous drainage

- pampiniform plexus drains into the ovarian veins
    - right ovarian vein drains into the inferior vena cava
    - left ovarian vein drains into the left renal vein

Lymphatic drainage

- drain alongside the ovarian vessels either to para-aortic nodes, or
- follow para-uterine vessels to iliac nodes, or

- alternative routes include inguinal nodes via round ligament or reaching the contralateral ovary by passing across the fundus of the uterus

Innervation

- sympathetic supply from T10 and T11 spinal segments via aorticorenal plexus and its branches
- parasympathetic supply from inferior hypogastric plexus via the uterine artery responsible for vasodilatation
- sensory fibers accompany sympathetic nerves

1.2: Ultrasound features

- first-line investigation
- homogeneous echotexture with a central echogenic medulla
- volume on ultrasound can be calculated with the following formula [5] :
    - 0.523 × length (cm) × width (cm) × depth (cm)
    - volume is expressed in cubic centimeters (cm^3)

1.3: Polycystic ovary syndrome (PCOS)

It is a complex condition characterized by elevated androgen levels, menstrual irregularities, and/or small cysts on one or both ovaries.[6] The disorder can be morphological (polycystic ovaries) or predominantly biochemical (hyperandrogenemia). Hyperandrogenism, a clinical hallmark of PCOS, can cause inhibition of follicular development, microcysts in the ovaries, anovulation, and menstrual changes.[7]

According to the Rotterdam consensus[12] ,polycystic ovarian syndrome (PCOS) is defined by the presence of two of three of the following criteria: oligo-anovulation, hyperandrogenism and polycystic ovaries (≥ 12

follicles measuring 2-9 mm in diameter and/or an ovarian volume > 10 mL in at least one ovary) based on greyscale ultrasound image.[13,14]

PCOS is a heterogeneous disorder that affects at least 7% of adult women.[8]

Research suggests that 5% to 10% of females 18 to 44 years of age are affected by PCOS, making it the most common endocrine abnormality among women of reproductive age in the U.S.[9] Women seeking help from health care professionals to resolve issues of obesity, acne, amenorrhea, excessive hair growth, and infertility often receive a diagnosis of PCOS.

1.4: Clinical feature and diagnosis of PCOS

Clinical sign include elevated luteinizing hormone (LH) , whereas follicular-stimulating hormone (FSH) levels are muted or unchanged.[10] Although signs and symptoms vary, the three most common factors associated with PCOS include ovulation irregularities, increased androgen levels, and cystic ovaries.[9,11] Problems with ovulation and elevated androgen levels occur in the majority of women with PCOS.[11] Moreover, hirsutism, acne, and alopecia are directly associated with elevated androgen levels, and the prevalence of polycystic ovaries on pelvic ultrasound exceeds 70% in patients with PCOS.[11]

Ultrasound evaluation of the ovarian morphology is essential for diagnosis of PCOS, since the laboratory and clinical Ultrasound evaluation of the ovarian morphology is essential for diagnosis of PCOS, since the laboratory and clinical features may not be observed in all patients. Today, transvaginal ultrasound is the most common modality for PCOS diagnosis which can provide new morphological and pathophysiological data on uterine and ovarian arteries. [15,16]

Colour Doppler sonography (CDS) is an ultrasound imaging which shows the amount of blood flow in vessels and tissues, and measures some criteria such as uterine and ovarian artery resistance indices (RI).[17] Uterine and ovarian artery RIs can give additional information on pathophysiology of the syndrome and can be applied as a diagnostic criterion in suspected cases of PCOS. Additional investigation and follow-

up of patients after medication and repeating the CDS might offer a deeper insight into PCOS treatment. [18]

Given the scarcity of studies on this subject, particularly in Iraq, and their conflicting results, also due to high incidence of PCOS and significance of early diagnosis and treatment of this disorder, this study aims to determine the differences in ovarian stromal blood flow between women with PCOS and healthy cases. Also in this study, variables such as endocrine tests and severity of hirsutism and acne were assessed to determine their relationship with uterine and ovarian artery RI in the patients with PCOS.

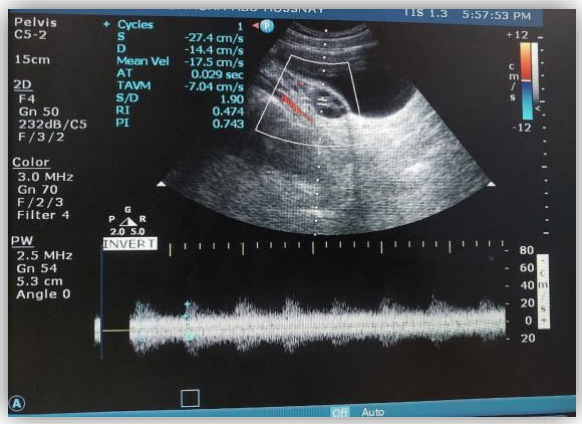
2. Patient And Methods:

This cross-sectional study was performed on 20 PCOS patients (PCOS group) and 20 healthy women (control group), referring to Al-batoul teaching Hospital of Diyala, Iraq. The participants were selected through convenience sampling. The appropriate sample size was calculated to be 12 cases in each group, with 95% confidence and power of 90%; however, for greater certainty we performed the study with two groups of 20 participants.

After obtaining written consent from the participants, all the women with PCOS were introduced to the research assistant and their demographic information including age, body mass index (BMI), levels of follicle stimulating hormone (FSH) and luteinizing hormone (LH), severity of hirsutism and acne were gathered and recorded in checklists. Then, in

the presence of the researchers, CDS of uterus and ovaries was performed in the early follicular phase using an ultrasound device(Philips EPIQ 7 Ultrasound Machine)

The ovarian stromal blood flow was measured and instead of measuring the blood flow of the ovarian parenchyma, ovarian artery RI of one of the vessels, as well as uterine artery RI were assessed using one of the ascending branches in the lateral of the cervix, in sagittal view. Using grayscale ultrasound, the size of ovaries, the number of follicles, ovarian stromal echogenicity, stromal thickness and the size of follicles were obtained and recorded in checklists. Additionally, these information were obtained and recorded from the control group, as well. Severity of hirsutism was determined based on Ferriman Gallwey Score[24] and acne severity was determined based on the number, type and distribution of skin lesions. [25]



Statistical analysis: The normality of numerical parameters were assessed by Kolmogorov-Smirnov and Shapiro-Wilk test. It was provided as Mean±SD since all markers fit both tests (there was no statistically significant difference). Student T test was used to compare the means of the numerical variables. The Pearson-Chi- square test was used to determine whether there were any significant differences in the percentage frequencies of the other parameters. To conduct present analyses, the statistical software packages SPSS version 25.0 and GraphPad Prism version 6 were used .

3. Inclusions and Exclusions criteria :

Inclusions criteria:

- Age range from menarche to 30 years old.
- BMI >+2 SDS (WHO Criteria) for PCOS group.
- People who had full hormonal analysis.
- The inclusion criteria for the control group were no symptoms. relevant to PCOS, menstrual disorder or infertility.
- People who had no surgical history.

Exclusions criteria:

- Individuals with systemic conditions include: (1) hypertension above 140/90 mmHg; (2) increased blood lipids; (3) hyperprolactinemia.
- People with metabolic diseases included (1) diabetes; (2) thyroid problems; (3) adrenals; (4) insulin resistance; (5) acanthose HAIRAN syndrome: hyperandrogenic insulin-resistant acanthosis nigricans.
- Consumers of anti-lepitic drugs such as: (1) Valproic acid; (2) high-dose exogenous androgens; (3) oral contraceptive pills.
- Individuals with androgen-secreting tumors.
- Subjects with congenital adrenal hyperplasia.
- People with Cushing's syndrome and people who have undergone hormonal treatments during the past 6 months.

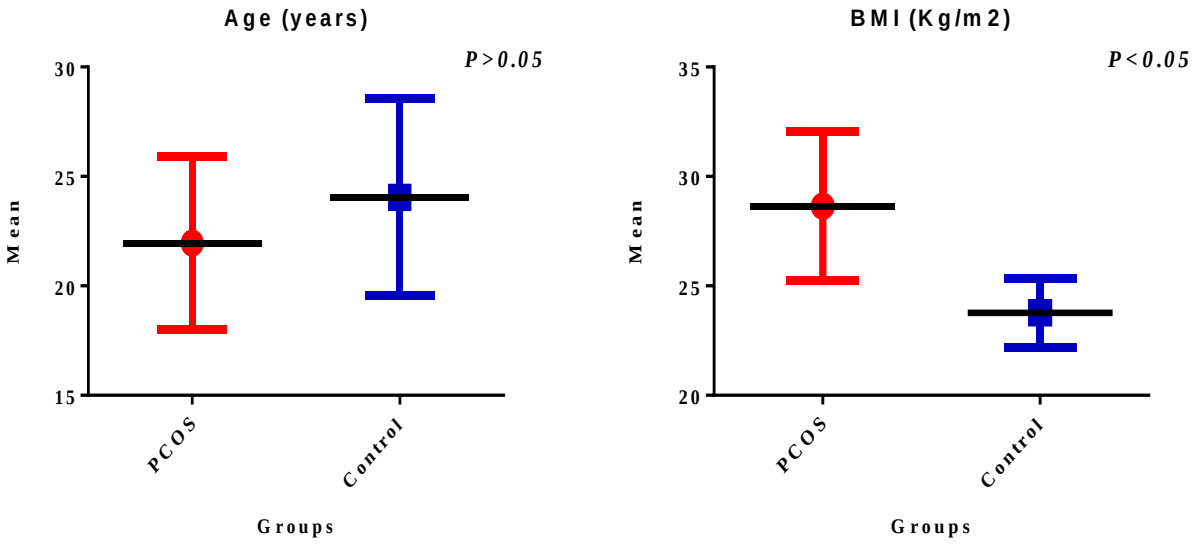
4. Results:

Results of present study showed there is significant difference ($p<0.05$) between BMI, FSH, LH markers and study groups. Mean levels of BMI,

FSH, LH markers were high in PCOS (28.65±3.42, 8.57±1.51, and 16.09±4.25) than control (23.77±1.58, 4.72±0.79, and 6.87±0.86) respectively. In contrast, the present study showed there is no significant different (p>0.05) between age and study groups (table and figure 1).

Table 1; The comparison of age, body mass index (BMI), follicle stimulating hormone (FSH) and luteinizing hormone (LH) in women with polycystic ovary syndrome (PCOS) and healthy women.

Groups		N	Mean	SD	P Value
Age	PCOS	20	21.95	3.94	P>0.05
	Control	20	23.05	4.51	
BMI	PCOS	20	28.65	3.42	P<0.05*
	Control	20	23.77	1.58	
FSH	PCOS	20	8.57	1.51	P<0.05*
	Control	20	4.72	0.79	
LH	PCOS	20	16.09	4.25	P<0.001***
	Control	20	6.87	0.86	



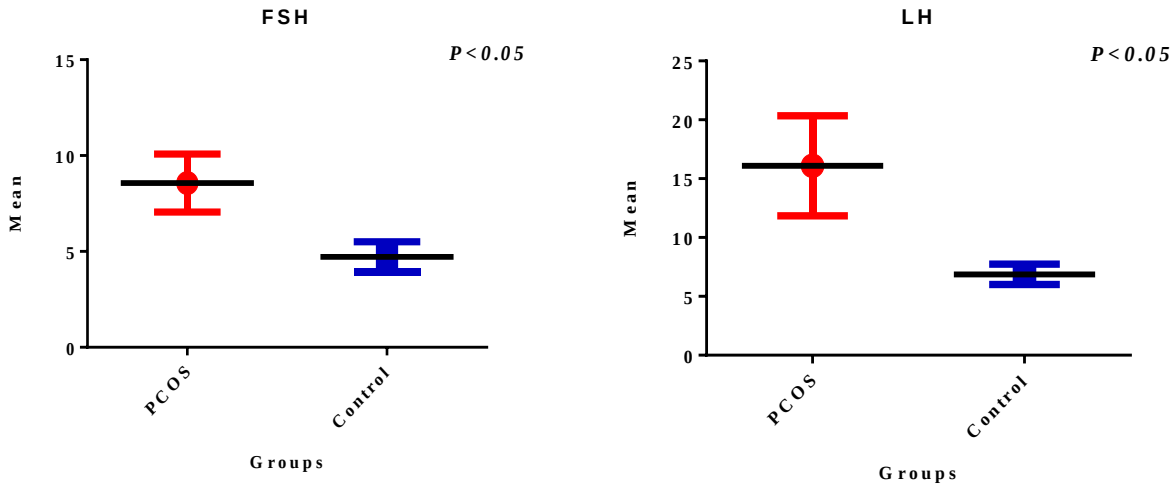


Figure 1; The comparison of age, body mass index (BMI), follicle stimulating hormone (FSH) and luteinizing hormone (LH) in women with polycystic ovary syndrome (PCOS) and healthy women.

Results of present study showed there is significant different ($p<0.05$) between hirsutism, acne, menstrual cycle and study groups. PCOS patients with sever hairsutism scored highest percentage (50.0%) than mild hairsutism that scored lowest percentage (20.0%), while in control group the normal hairsutism scored highest percentage (80.0%) and sever hairsutism scored lowest percentage (0.0%). No and sever acne scored highest percentage (30.0% and 35.0%) in PCOS patients compared to control group that have (85.0%) No acne and (0.0%)sever acne. Finally, (85.0%) of PCOS patients have Oligomenorrhea menstrual cycle and (15.0%) have normal menstrual cycle, where as in control group (90.0%) have normal menstrual cycle and (10.0%) have oligomenorrhea menstrual cycle (table 2).

Table 2; Comparison of hirsutism , acne Severity, and menstrual cycle in women with polycystic ovary syndrome (PCOS) and healthy women

			Groups		Total	p value
			PCOS (N=20)	Control (N=20)		
Hirsutism	Normal	n	4	16	20	p<0.001***
		%	20.0%	80.0%	50.0%	
	Mild	n	2	3	5	
		%	10.0%	15.0%	12.5%	
	Moderate	n	4	1	5	
		%	20.0%	5.0%	12.5%	
	Sever	n	10	0	10	
		%	50.0%	0.0%	25.0%	
Acne	No acne	n	6	17	23	p<0.01**
		%	30.0%	85.0%	57.5%	
	Mild	n	5	2	7	
		%	25.0%	10.0%	17.5%	
	Moderate	n	2	1	3	
		%	10.0%	5.0%	7.5%	
	Sever	n	7	0	7	
		%	35.0%	0.0%	17.5%	
Menstrual cycle	Normal	n	3	18	21	p<0.001***
		%	15.0%	90.0%	52.5%	
	Oligomenorrhea	n	17	2	19	
		%	85.0%	10.0%	47.5%	

Results of present study showed there is significant difference ($p<0.05$) between Right Ovarian Volume (ml), Left Ovarian Volume (ml), Right Ovarian Artery RI, left ovarian artery RI, Left Uterine Artery RI, Right Uterine Artery RI markers and study groups. Mean levels of right Ovarian Volume (ml) and Left Ovarian Volume (ml) markers were high in PCOS (11.31±1.49, and 11.21±1.45) than control (6.67±0.72, and

6.39±0.78) . In contrast, mean levels of Right Ovarian Artery RI, left ovarian artery RI, Left Uterine Artery RI, Right Uterine Artery RI markers were low in PCOS (0.64±0.16, 0.65±0.16, 0.72±0.14 and 0.71±0.15) than control (0.70±0.06, 0.69±0.06, 0.84±0.07 and 0.83±0.06) (table 3 and figure 2).

Table 3; Comparison of ovarian volumes, ovarian and uterine artery resistance indices (RI) on both sides in the polycystic ovary syndrome (PCOS) and control groups

Groups		N	Mean	SD	P Value
Right Ovarian Volume (ml)	PCOS	20	11.31	1.49	P<0.001***
	Control	20	6.67	0.72	
Left Ovarian Volume (ml)	PCOS	20	11.21	1.45	P<0.001***
	Control	20	6.39	0.78	
Right Ovarian Artery RI	PCOS	20	0.64	0.16	P<0.05*
	Control	20	0.70	0.06	
left ovarian artery RI	PCOS	20	0.65	0.16	P<0.05*
	Control	20	0.69	0.06	
Left Uterine Artery RI	PCOS	20	0.72	0.14	P<0.01**
	Control	20	0.84	0.07	
Right Uterine Artery RI	PCOS	20	0.71	0.15	P<0.01**
	Control	20	0.83	0.06	

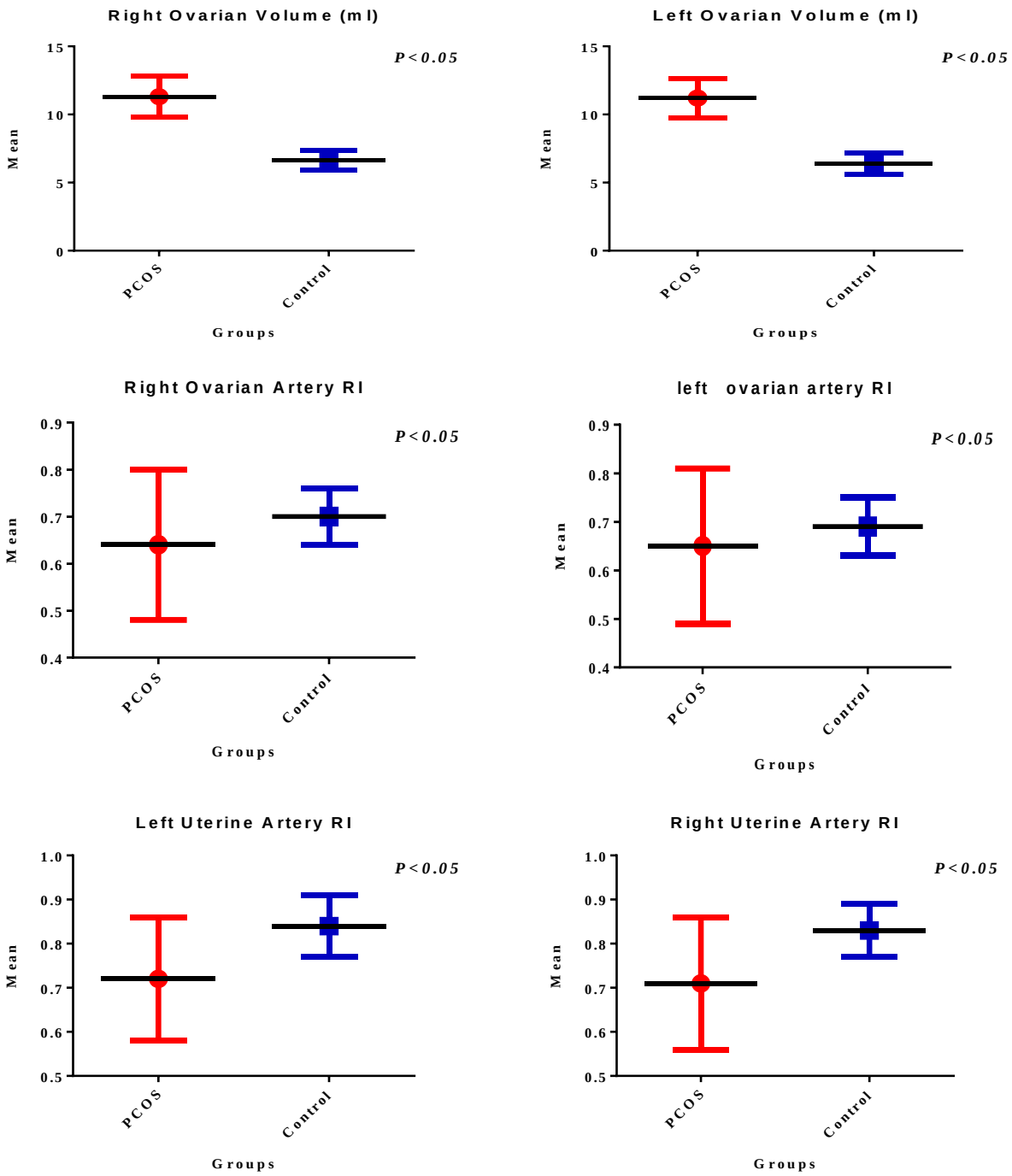


Figure 2; Comparison of ovarian volumes, ovarian and uterine artery resistance indices (RI) on both sides in the polycystic ovary syndrome (PCOS) and control groups

5. Discussion

The present study revealed no significant different between age of study groups, and cause of it may be due to sample size. The current study showed a high incidence of polycystic ovary disease in females more than 18 years and these report are compatible to results Wendland et al., (2021) that showed high prevalence of PCOS patients in women more than 18 years. Because the diagnostic criteria for PCOS may change, or even normalize, during the course of a woman's reproductive life, the prevalence of PCOS appears to decline with age (Kim et al., 2021). Previous results reflect that age-stratified thresholds demonstrate superior diagnostic performance, with an improved balance of sensitivity and specificity compared with a single threshold. Authors propose age-specific thresholds for better diagnostic performance (Ahmad et al., 2021). The present study showed high BMI levels in PCOS patients than controls, and these results matched with results Guan et al., (2020). Obesity further augments the adverse metabolic and reproductive outcomes of PCOS . Obesity increases insulin resistance and compensatory hyperinsulinemia, which in turn increases adipogenesis and decreases lipolysis. Obesity sensitizes thecal cells to LH stimulation and amplifies functional ovarian hyperandrogenism by upregulating ovarian androgen production. Obesity increases inflammatory adipokines which, in turn, then promote hyperinsulinemia, which increases obesity, providing a vicious feedback cycle. Obesity increases insulin resistance and compensatory hyperinsulinemia, glucose intolerance, dyslipidemia, and increases risk of pregnancy complications (Glueck and Goldenberg, 2019).

Obese women with PCOS have a more severe phenotype than those less obese, with more severe menstrual irregularity, infertility, miscarriage, pregnancy induced hypertension, gestational diabetes, prematurity, biochemical and clinical hyperandrogenism, glucose intolerance and/or T2DM, and metabolic syndrome (Barber, 2022).

The present study showed high levels of FSH and LH in PCOS patients than controls, and these results matched with results Tefagh et al., (2022). There are numerous of hypothesis about the causes of PCOS development and the concurrent presence of several inter dependent disorders. In obese girls this disorder arises as an exaggerated adrenarche, according to suggestion of a group of experts. The combination of elevated levels of adrenal androgen and obesity leads to increased formation of extra glandular estrogen by the way of peripheral aromatization. This high amount of estrogen exerts appositive feedback on LH secretion and reverse in FSH secretion (Racoubian et al., 2020). The increase in LH level increases ovarian androgen production (Hashemi et al., 2016).

Forslund et al., (2021) showed the FSH levels increased in the PCOS group during the 32 years of follow-up, but not during the last 11 years. However, FSH was persistently lower in women with PCOS from perimenopause up to senescence, compared with controls. This finding agrees with previous findings in perimenopausal women with PCOS from another cohort that was diagnosed later, in 1992 (Forslund et al., 2019). That cohort was diagnosed during their reproductive age and reexamined at a mean age of 52 years, when FSH levels were lower compared with controls (Forslund et al., 2021). There exists some experimental evidence that increased FSH may be related to adiposity. Studies in the mouse have shown that

neutralization of FSH action, by blocking antibodies, reduce adiposity, possibly by action of enzymes regulating lipogenesis and conversion of white adipocytes to brown adipocytes (Mao et al., 2022). The mechanism of the remaining lower FSH levels after the menopause is not known. Because, in fertile women with PCOS, the gonadotropin-releasing hormone (GnRH) pulse frequency in the hypothalamus differs from that in healthy controls , it could be speculated that the lower FSH level in PCOS women at higher ages may reflect a remaining difference in hypothalamic function, perhaps primed earlier to an abnormal GnRH pulse frequency, possibly due to genetic differences (Singh et al., 2023).

It has been suggested that the majority of PCOS patients with hyperandrogenism suffer from LH secretion problems, which lead to abnormal folliculogenesis and failed dominant follicle selection (Zeng et al., 2020). In obese PCOS patients on a restricted diet, evidence of estradiol-dependent negative feedback on LH secretion retention can predict follicle maturation and ovulation. In the pathophysiology of polycystic ovarian disease, abnormality of the hypothalamic-pituitary-or adrenal axis has been imposed. In women with PCOS, the pituitary-derived luteinizing hormone (LH) is often usually elevated, which stimulates ovarian androgen overproduction (Milewicz et al., 2018).

Recent data suggests that the body mass index was not correlated with increased LH/FSH ratio. Since LH/FSH ratio was the same in normal BMI women, healthcare professionals need to think about ways to normalize this ratio beyond weight reduction (Saadia, 2020).

The value of serum Anti-Muller hormone concentration has been found not significantly superior to LH/FSH ratio in PCOS diagnosis. Although these biomarkers separately are not adequate for PCOS diagnosis based on their own value, the combination of different endocrine factors including AMH, LH and LH/FSH ratio together with BMI and other anthropometric and clinical characteristics may offer extra value to establish the diagnosis of PCOS (Le et al., 2019).

Women with PCOS often experience dermatologic manifestations of hyperandrogenism, including hirsutism, acne vulgaris, and androgenic alopecia. Hirsutism was measured with different tools in 1987, 2008, and 2019, and can therefore not be compared directly. However, hirsutism gradings have shown good correlation between objective and subjective measurements (FRANKS, 1989), and interestingly, the hirsutism ratio between women with PCOS and controls was similar at all times, whereas the ratio of biochemical androgens decreased with increasing age. The reason for maintained hirsutism throughout life in PCOS women without a biochemical explanation is not known. One hypothesis might be that genetic factors correlated to androgen receptor activity or 5α-reductase activity (the enzyme that converts testosterone to dihydrotestosterone) is linked to PCOS and this phenotypical finding. Another hypothesis could be sensitization of androgen receptors in hair follicles earlier in life (Forslund et al., 2021).

The presence of polycystic ovaries in the acne patients did not correlate with acne severity, infertility, menstrual disturbance, hirsutes, or biochemical endocrinological abnormalities (Sharma et al., 2019). Despite

the presence of heterogeneity and publication bias among available literature, it may be concluded that acne is one of the common dermatological manifestations in PCOS (Ramezani Tehrani et al., 2021). Acne in people with confirmed polycystic ovarian syndrome may be exacerbated by hyperadrogenism potentially resulting in persistent or recurrent acne (UK, 2021). Hyperinsulinism and resultant hyperandrogenism in PCOS chronically alter gonadotropin secretion, leading to increased LH and disruptions in the normal pituitary-ovarian axis, which can manifest as oligoamenorrhea, infertility, obesity, hirsutism, acne, frequent hypertension, and hyperlipidemia . The central role of hyperinsulinemia in PCOS has provided an impetus toward the development of treatments for PCOS that lower insulin levels. Metformin, a biguanide hypoglycemic drug, improves insulin levels and insulin sensitivity and has been shown to be a safe and well-tolerated treatment for adult women with PCOS, with minimal side effects and without reported lactic acidosis (Shamim et al., 2022).

Previous study showed oligoovulatory women with PCOS and overt oligo/amenorrhea have greater degrees of insulin resistance (IR) but not hyperandrogenism (HA) when compared with oligo-ovulatory eumenorrheic women with PCOS, suggesting that insulin resistance (IR) and hyperinsulinemia but not HA play a role in determining the degree of menstrual dysfunction, which can be used as a clinical marker for the degree of IR in oligo-ovulatory PCOS (Ezeh et al., 2021).

Results of present study showed high volume of right and left ovarian of patients with PCOS than controls and these results compatible to results

Chawla and Anand (2020). Farshchian et al., (2015) showed the right and left ovarian artery RI were low in patients POCS than controls and these results agreed with present results. Previous study showed there seem to be significant differences in ovarian stromal and uterine artery blood flows in women with PCOS as compared to healthy women which may partly be explained by the characteristic hormonal variations in PCOS, such as hyperinsulinemia, raised LH and Testosterone levels. Furthermore, alterations in blood flow may be responsible for certain adverse effects such as recurrent spontaneous abortion, infertility, and ovarian hyper stimulation syndrome (OHSS) that are often seen in women suffering from this condition. Doppler analysis may help in understanding the etiology and clinical implications of PCOS and provide us with an additional parameter for ultrasonographic diagnosis of PCOS, thus improving the sensitivity for detecting this condition (Chawla and Anand, 2020).

Doppler ultrasonographic indices are found significantly different in women with ovarian dysfunction from those of normal women. Doppler indices have significant correlations with the number of antral follicles, testosterone, dehydroepiandrosterone, LH, and AMH. Available data also shows that hirsutism and insulin resistance have correlations with pulsatility index (PI). These results support the use of Doppler ultrasonography for the examination of ovarian blood flow abnormalities (Wang et al., 2023).

In general, androgens were found to correlate positively with FI, VI, and VFI, but negatively with PI and RI in women with PCOS in the results Wang et al., (2023). In women with normal menstrual cycles, testosterone

correlates with retrieved oocytes (Aslam et al., 2022). Many studies have found that 3D Doppler ultrasonographic blood flow indices are different in women with PCOS and normal women (Al-Rab et al., 2015). It is suggested that increased ovarian blood flow in PCOS patients, which is also observed in normal ovaries, may affect, or may be affected by androgen levels directly or indirectly (Rodriguez Paris and Bertoldo, 2019). Kupesic et al. (2002) found a strong positive correlation (r=0.793) between the estradiol levels and flow index (FI) in women undergoing vascularization flow index (VFI). Wang et al., (2023) found significant negative correlations (r=−0.33) between estradiol levels and pulsatility index (PI) in PCOS patients.

Among the included studies, Kupesic et al. (2002) found a stronger negative correlation (r=−0.67) between follicle stimulating hormone (FSH) and flow index (FI) in infertile women with normal FSH levels who underwent vascularization flow index (VFI) procedures. Al-Rab et al., (2015) found no correlation between FSH and either FI or vascularization index (VI) in PCOS patients. Nyström et al. (2019) found strong negative correlations between FSH and ovarian volume, antral follicle count, peak flow velocity and end-diastolic peak velocity in infertile women. Authors found fewer studies to report the correlations between AMH and Doppler ultrasonography measures. Wang et al., (2023) found significant positive correlations between AMH levels and vascularization index (VI) and FI in women with PCOS.

Doppler ultrasonography of ovarian stromal vascularization provides additional support for the diagnosis of PCOS (He et al., 2020). Doppler ultrasonographic studies demonstrate that blood flow is increased during

the early stages of the follicular phase and reaches a peak at ovulation among women with spontaneous cycles but this pattern is altered in pathological conditions (Zhou et al., 2019). It is suggested that 3D Doppler ultrasonography can help in individualizing treatment for women with a smaller number of antral follicles, smaller ovarian volume, and lower ovarian vascularization, who can be considered for initial higher doses of gonadotropins and longer treatment schedule . In comparison with 2D Doppler ultrasonography, 3D Doppler ultrasonography is more expensive, but it has several uses to study ovarian dysfunction such as follicular count, echogenicity of total ovary/stroma, ovarian volume, and blood flow (Wang et al., 2023).

6. Conclusions

According to the color doppler sonography findings, ovarian stromal and uterine blood flow parameters were significantly different in the PCOS and control groups.

7. Recommendations:

I suggest to include the Doppler study for patient with polycystic ovary syndrome as a routine investigation in clinical work and recommend further study on this subject.

8. References:

1. FIPAT. Terminologia Anatomica. 2nd Ed. FIPAT.library.dal.ca. Federative International Programme for Anatomical Terminology, 2019.
2. Stephanie Ryan, Michelle McNicholas, Stephen J. Eustace. Anatomy for Diagnostic Imaging. (2018)
3. Paul Butler, Adam Mitchell, Jeremiah C. Healy. Applied Radiological Anatomy. (2012)
4. Foshager MC, Walsh JW. CT anatomy of the female pelvis: a second look. (1994) Radiographics : a review publication of the Radiological Society of North America, Inc. 14 (1): 51-64; discussion 64-6.
5. Saksouk FA, Johnson SC. Recognition of the ovaries and ovarian origin of pelvic masses with CT. Radiographics. 2004;24 Suppl 1 : S133-46.
6. Umland EM, Weinstein LC, Buchanan EM. Menstruation-related disorders. In: DiPiro JT, Talbert RL, Yee GC, et al., editors. Pharmacotherapy: A Pathophysiologic Approach. 8th ed. New York: McGraw-Hill; 2011. p. 1393.
7. Lin LH, Baracat MC, Gustavo AR, et al. Androgen receptor gene polymorphism and polycystic ovary syndrome. Int J Gynaecol Obstet. 2013;120:115–118.
8. Aubuchon M, Legro RS. Polycystic ovary syndrome: Current infertility management. Clin Obstet Gynecol. 2011;54(4):675–684.
9. American Congress of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 108: Polycystic Ovary Syndrome. Obstet Gynecol. 2009;114(4):936–949.
10. Urbanek M. The genetics of polycystic ovary syndrome. Natl Clin Pract Endocrinol Metab. 2007;3:103–111.
11. Azziz R, Carmina E, Dewailly D, et al. Position statement: Criteria for defining polycystic ovary syndrome as a predominantly hyper-androgenic syndrome. An Androgen Excess Society guideline. J Clin Edocrinol uMetab. 2006;91:4237–4245.
12. Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group . Revised 2003 consensus on diagnostic criteria and long-term health

risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19(1): 41–7.

13. Järvelä IY, Mason HD, Sladkevicius P, Kelly S, Ojha K, Campbell S, et al. Characterization of normal and polycystic ovaries using three – dimensional power Doppler ultra sonography. J Assist Reprod Genet. 2002;19(12):582-90.
14. Pan HA, Wu MH, Cheng YC, Li CH, Chang FM. Quantification of doppler signal in polycystic ovary syndrome using three dimensional power doppler ultrasonography an possible new marker for diagnosis. Hum Reprod. 2002;17(1):201-6.
15. Lam PM, Johnson IR, Raine-Fenning NJ. Three-dimensional ultrasound features of the polycystic ovary and the effect of different phenotypic expressions on these parameters. Hum Reprod. 2007;22(12):3116-23.
16. Bostancia MS, Sagsoz N, Noyanb V, Yucel A, Goren K. Comprasion of ovarian stromal and uterine Artery Blood flow measured by color Doppler ultra sonography in polycystic ovary syndrome patients and patients with ultra sonographic evidence of polycystic. J Clin Gynecol Obstet. 2013;2(1):20-6.
17. Aleem FA, Predanic M. Transvaginal color Doppler determination of the ovarian and uterine blood flow characteristics in polycystic ovary disease. Fertile Steril. 1996;65(3):510-6.
18. Lee TT, Rausch ME. Polycystic ovarian syndrome: role of imaging in diagnosis. Radiographics. 2012;32(6):1643-57.
19. Battaglia C, Artini PG, Salvatori M, Giulini S, Petraglia F, Maxia N, etal. Ultrasonographic patterns of polycystic ovaries :Color Doppler and hormonal correlations. Ultrasound Obstet Gynecol.1998;2(1):50-6.
20. Dolz M, Osborne NG, Blanes J, Raga F, Abad-Velasco L, Villalobos A, et al. Polycystic ovarian syndrome : assessment with color Doppler angiography and three-dimensional ultrasonography. J Ultrasound Med. 1999;18(4):303-13.

21. Resende AV, Mendes MC, Dias de Moura M, Mendonça HC, Gomes Premoli AC, Reis RM, et al. Doppler study of the Uterine arteries and ovarian stroma in patients with polycystic ovary syndrome. Gynecol Obstet Iavest. 2001;52(3):153-7.
22. Ng EH, Chen CC, Yeung WS, Ho PC. Comparsion of ovarian stromal blood flow between fertile women with normal ovaries and infertile women with polycystic ovary syndrome. Hum Reprod. 2005;20(1):1881-6.
23. Adali E, Kolusari A, Adali F, Yildizhan R, Kudoglu M, Sahin HG. Doppler analysis of uterine perfusion and ovarian stromal blood flow in polycystic ovary syndrome. Int J Gynaecol Obstet. 2009; 105(2):154-7.
24. Zaidi J, Jacobs H, Cambell S, Tan SL. Blood flow changes in the ovarian and uterine arteries in women with polycystic ovary syndrome who respond to clomiphene citrate:Correlation with serum hormone concentrations. Ultrasound Obstet Gynecol.1998;12(3)188-96.
25. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab 1961;21:1440-7.
26. Ahmad, A. K., Quinn, M., Kao, C. N., Greenwood, E., Cedars, M. I., & Huddleston, H. G. (2019). Improved diagnostic performance for the diagnosis of polycystic ovary syndrome using age-stratified criteria. *Fertility and sterility*, *111*(4), 787-793.\
27. Al-Rab, M. T. G., Mohammed, A. B. F., Mo'men, M. H., & Razek, M. A. (2015). Three-dimensional power Doppler indices of ovarian stromal blood flow and serum vascular endothelial growth factor after laparoscopic ovarian drilling in women with polycystic ovary syndrome. *Middle East Fertility Society Journal*, *20*(3), 138-143.
28. Aslam, A., Khadija, S., Aslam, A., Shaukat, S., Irshad, A., & Tariq, S. (2022). The Role of Colour Doppler Imaging in the Diagnosis of Poly Cystic Ovarian. Syndrome: Colour Doppler Imaging in PCOS. *Pakistan BioMedical Journal*, 157-160.
29. Barber, T. M. (2022). Why are women with polycystic ovary syndrome obese?. *British Medical Bulletin*, *1*, 11.

30. Chawla, K., & Anand, R. (2020, January). Role of Color Doppler ultrasonography in evaluation of women with Polycystic Ovarian Syndrome (case control study). European Congress of Radiology-ECR 2020.
31. Ezeh, U., Ezeh, C., Pisarska, M. D., & Azziz, R. (2021). Menstrual dysfunction in polycystic ovary syndrome: association with dynamic state insulin resistance rather than hyperandrogenism. *Fertility and Sterility*, *115*(6), 1557-1568.
32. Farshchian, N., Fakheri, T., & Hezbi, A. (2015). A Comparison of Color Doppler Sonography Findings in Polycystic Ovarian Syndrome Patients and Healthy Women. *Journal of Babol University of Medical Sciences*, *17*(11), 61-66.
33. Forslund, M., Landin-Wilhelmsen, K., Schmidt, J., Brännström, M., Trimpou, P., & Dahlgren, E. (2019). Higher menopausal age but no differences in parity in women with polycystic ovary syndrome compared with controls. *Acta obstetricia et gynecologica Scandinavica*, *98*(3), 320-326.
34. Forslund, M., Schmidt, J., Brännström, M., Landin-Wilhelmsen, K., & Dahlgren, E. (2021). Reproductive hormones and anthropometry: a follow-up of PCOS and controls from perimenopause to older than 80 years. *The Journal of Clinical Endocrinology & Metabolism*, *106*(2), 421-430.
35. FRANKS, S. (1989). Polycystic ovary syndrome: a changing perspective. *Clinical endocrinology*, *31*(1), 87-120.
36. Glueck, C. J., & Goldenberg, N. (2019). Characteristics of obesity in polycystic ovary syndrome: Etiology, treatment, and genetics. *Metabolism*, *92*, 108-120.
37. Guan, Y., Wang, D., Bu, H., Zhao, T., & Wang, H. (2020). The effect of metformin on polycystic ovary syndrome in overweight women: a systematic review and meta-analysis of randomized controlled trials. *International journal of endocrinology*, *2020*.
38. Hashemi, A. H., Mozdarani, H., & Naghavi, A. (2016). Comparison of the levels of LH and FSH, TSH, prolactin, progesterone and estradiol hormones between Iranian infertile women with polycystic ovary syndrome and healthy women. International Journal of Medical Research & Health Sciences, *5*(12), 370-375.(199).
39. He, G., Zhao, J., Yang, Z., Zhao, Z., Bai, Y., & Xiong, W. (2020). Comparison of image features and diagnostic value of color Doppler ultrasound and two-dimensional

ultrasound in the diagnosis of ovarian sex cord-stromal tumors. *Oncology Letters*, *20*(2), 1671-1676.

40. Kim, K., Pollack, A. Z., Nobles, C. J., Sjaarda, L. A., Zolton, J. R., Radoc, J. G., ... & Mumford, S. L. (2021). Associations between blood cadmium and endocrine features related to PCOS-phenotypes in healthy women of reproductive age: a prospective cohort study. *Environmental Health*, *20*(1), 64.
41. Kupesic, S. A. N. J. A., & Kurjak, A. (2002). Predictors of IVF outcome by three-dimensional ultrasound. *Human reproduction*, *17*(4), 950-955.
42. Le, M. T., Le, V. N. S., Le, D. D., Nguyen, V. Q. H., Chen, C., & Cao, N. T. (2019). Exploration of the role of anti-Mullerian hormone and LH/FSH ratio in diagnosis of polycystic ovary syndrome. *Clinical Endocrinology*, *90*(4), 579-585.
43. Mao, L., Wang, L., Bennett, S., Xu, J., & Zou, J. (2022). Effects of follicle-stimulating hormone on fat metabolism and cognitive impairment in women during menopause. *Frontiers in Physiology*, *13*, 2557.
44. Milewicz, A., Kudła, M., Spaczyński, R. Z., Dębski, R., Męczekalski, B., Wielgoś, M., ...& Zachurzok, A. (2018). The polycystic ovary syndrome: a position statement from the Polish Society of Endocrinology, the Polish Society of Gynaecologists and Obstetricians, and the Polish Society of Gynaecological Endocrinology. Endokrynologia Polska, 69(4), 328-344.
45. Nyström, A., Mörse, H., Nordlöf, H., Wiebe, K., Artman, M., Øra, I., ... & Elfving, M. (2019). Anti-müllerian hormone compared with other ovarian markers after childhood cancer treatment. *Acta Oncologica*, *58*(2), 218-224.
46. Racoubian, E., Aimagambetova, G., Finan, R. R., & Almawi, W. Y. (2020). Age-dependent changes in anti-Müllerian hormone levels in Lebanese females: correlation with basal FSH and LH levels and LH/FSH ratio: a cross-sectional study. BMC Women's Health, 20(1), 1-6.
47. Ramezani Tehrani, F., Behboudi-Gandevani, S., Bidhendi Yarandi, R., Saei Ghare Naz, M., & Carmina, E. (2021). Prevalence of acne vulgaris among women with polycystic ovary syndrome: a systemic review and meta-analysis. *Gynecological Endocrinology*, *37*(5), 392-405.

48. Rodriguez Paris, V., & Bertoldo, M. J. (2019). The mechanism of androgen actions in PCOS etiology. *Medical sciences*, *7*(9), 89.
49. Saadia, Z. (2020). Follicle stimulating hormone (LH: FSH) ratio in polycystic ovary syndrome (PCOS)-obese vs. Non-obese women. *Medical Archives*, *74*(4), 289.
50. Shamim, H., Jean, M., Umair, M., Muddaloor, P., Farinango, M., Ansary, A., ... & Mohammed, L. (2022). Role of Metformin in the Management of Polycystic Ovarian Syndrome-Associated Acne: A Systematic Review. *Cureus*, *14*(8).
51. Sharma, S., Mathur, D. K., Paliwal, V., & Bhargava, P. (2019). Efficacy of metformin in the treatment of acne in women with polycystic ovarian syndrome: a newer approach to acne therapy. *The Journal of clinical and aesthetic dermatology*, *12*(5), 34.
52. Singh, R., Kaur, S., Yadav, S., & Bhatia, S. (2023). Gonadotropins as pharmacological agents in assisted reproductive technology and polycystic ovary syndrome. *Trends in Endocrinology & Metabolism*.
53. Tefagh, G., Payab, M., Qorbani, M., Sharifi, F., Sharifi, Y., Ebrahimnegad Shirvani, M. S., ... & Ebrahimpur, M. (2022). Effect of vitamin E supplementation on cardiometabolic risk factors, inflammatory and oxidative markers and hormonal functions in PCOS (polycystic ovary syndrome): a systematic review and meta-analysis. *Scientific reports*, *12*(1), 5770.
54. UK, N. G. A. (2021). Management options for people with acne vulgaris and polycystic ovary syndrome.
55. Wang, W. Q., Chu, G. H., & Hou, X. X. (2023). A comparison of Doppler measures of ovarian blood flow between women with and without ovarian dysfunction and correlations of Doppler indices with ovarian dysfunction markers: a meta-analysis. *Annals of Translational Medicine*, *11*(2), 110-110.
56. Wendland, N., Opydo-Szymaczek, J., Mizgier, M., & Jarząbek-Bielecka, G. (2021). Subgingival microflora in adolescent females with polycystic ovary syndrome and its association with oral hygiene, gingivitis, and selected metabolic and hormonal parameters. Clinical Oral Investigations, 25(3), 1485-1496.

57. Zeng, X., Xie, Y.J., Liu, Y.T., Long, S.L. and Mo, Z.C., (2020). Polycystic ovarian syndrome: correlation between hyperandrogenism, insulin resistance and obesity. Clinica Chimica Acta, 502, pp.214-221.
58. Zhou, L., Xuan, Z., & Wang, Y. (2019). Diagnostic value of ultrasound score, color Doppler ultrasound RI and spiral CT for ovarian tumors. *Oncology letters*, *17*(6), 5499-5504.