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RESEARCH ARTICLE

CLINICAL FEATURES OF POLYCYSTIC OVARIAN SYNDROME (PCOS) IN RELATION TO SOME BIOCHEMICAL HORMONAL ASSESSMENT AND ULTRASOUND FINDINGS

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ABSTRACT

Fifty female patients at the reproductive age were subjected for evaluation and consultation at the infertility clinic. Their complete histories were recorded and included the type of infertility, duration, patient age, parity, gravity and menstrual abnormalities. For each, a general examination and special gynecological examination including concentration on evidence of Hirsutism, acne and obesity was considered. Blood samples were taken at early follicular phase of menstruation for Radioimmunoassay (RIA) to determine Luteinizing hormone (LH) and follicular stimulating hormone (FSH) levels. Trans-vaginal ultrasound was conducted during early follicular phase of menstrual cycle. Biochemical investigations on patients with PCOS showed that there is a direct relationship between ovarian size and stromal echogenicity. The PCOS presented with secondary infertility of 64%, while, it was 16% in the primary phase. PCOS was recorded more common in urban area (70%), while, it was 30% in rural area. The use of ultrasound is more accurate than biochemical investigations in the diagnosis of PCOS.

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INTRODUCTION

Polycystic ovarian syndrome (PCOS) represents a heterogeneous group of disorders characterized by a specialized ovarian morphology. It is a reproductive endocrinology problem rather than local ovarian diseases (Eden, 1991), as illustrated in Figure 1. It is the most common form of an-ovulatory infertility as well as association with menstrual disturbances with an alteration in hormonal parameters that leads many affected women at reproductive age (Zoe, 1998). There is a considerable evidence to suggest that the effect of PCOS may persist beyond the cessation of reproductive life with an increased risk of endometrial cancer, diabetes mellitus, hyperlipidemia and cardiovascular diseases (3). Several studies have suggested a prevalence of PCOS of 5-10% in women at reproductive age all over the world (Diamanti-Kandarakis, 1999). The pathogenesis of PCOS is poorly understood and the primary defect may be insulin resistance leading to hyperinsulinemia (Ibanez *et al.*, 2002). In the ovary, the cardinal feature is functional hyperandrogenism (Figure 2). Circulating concentrations of insulin and luteinizing hormone (LH) are generally raised. The theca cells, which envelop the follicle and produce androgens for conversion in the ovary to estrogen, are over-responsive to this stimulation (Norman, 2002).

They increase in size and over-produce androgens. The rise in LH is thought to be caused by the relatively high and unchanging concentrations of estrogens that may alter the control of this hormone by the hypothalamic-pituitary axis (Fox, 1994). This combination of raised levels of androgens, estrogens, insulin and LH explains the classic PCOS presentation of Hirsutism, an-ovulation or dysfunctional bleeding and dysfunction of glucose metabolism (Norman, 2002). The etiology of PCOS is uncertain, and there is some evidence of autosomal transmission related to strong familial clustering. Potentially, a gene or series of genes renders the ovaries susceptible to insulin stimulation of androgen secretion, while blocking follicular maturation (Dunaif, 2004). The genetic predisposition may be expressed as premature balding in men (Tsilchorozidou, 2004). The onset may occur in late childhood since many of the metabolic and endocrine features of the disorder mimic puberty (Hull, 1987). Insulin resistance increases dramatically at the onset of puberty and then declines in early adulthood. This increase in insulin resistance is associated with an increase in pulse amplitude of luteinizing hormone, increase in androgen concentration and irregular menses (Ehrmann, 1997). Multiple and small ovarian cysts are seen on ultrasound examination and are common and normal feature of puberty (Lees *et al.*, 1998). It is therefore possible that women are genetically predisposed to PCOS and fail to resume normal insulin sensitivity and continue to express metabolic and endocrine feature usually confined to

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puberty (Adams *et al.*, 1985). The diagnostic criterion of PCOS is controversial and is generally based on menstrual problem and infertility, clinical or biochemical hyperandrogenism and the presence of polycystic ovaries on ultrasound examination, Box 1. Patients with PCOS may complain several conditions, such as menstrual dysfunction (oligomenorrhea or amenorrhea), (Pasquali *et al.*, 1989), hyperandrogenism, infertility, obesity and diabetes mellitus (Dunaif, 1994). Physical examination may include hirsutism, obesity and acanthuses (Azziz, 1994).

Criteria of the US National Institutes of Health:-Criteria for PCOS and related disorders. PCOS: Presence of menstrual abnormalities and anovulation. Presence of clinical and /or biochemical hyperandrogenaemia. Absence of hyperprolactinaemia or thyroid diseases. Absence of late-onset congenital adrenal hyperplasia. Absence of Cushing's syndrome.

Polycystic ovaries: Presence of polycystic ovaries on ultrasound examination. Absence of menstrual or cosmetic symptoms. Absence of biochemical hyperandrogenaemia.

Idiopathic Hirsutism: Presence of excess hair growth

Certain laboratory tests may indicate the presence of PCOS, such as, LH/FSH ratio, prolactin level, serum estradiol and estrone, glucose tolerance, abnormal lipid profile, elevated androgen levels and decrease in sex hormone-binding globulin levels (Boots *et al.*, 1998). Ultrasound findings are performed with trans-abdominal transducer for the pelvic organs showed that the ovaries are identical as lozenge-shaped structures lateral to the uterus (Cherrenoak, 1993). Trans-vaginal ultrasound (TVUS) should be performed with an empty bladder to bring the uterine fundus and ovaries closer to the vaginal fornices, endovaginal transducer probe (Fox, 1999). TVUS is currently the preferred and the golden standard for diagnosing PCOS (Conway, 1992). The development of ultrasound imaging in PCOS included the following techniques; the three-dimensional ultrasound has been used to measure ovarian stromal volumes that provide information, which is not available from two-dimensional ultrasound (Adams, 1996). The Doppler ultrasound, which is the transvaginal color and pulse Doppler ultrasound in combination with B-mode imaging, is used as a non-invasive method to assess blood flow in both obstetrics and gynaecology. Color and power Doppler allow detection of the uterine and ovarian vessels as well as the network within the ovarian stroma (Fleischer, 1997). The spectral Doppler assessment of vascular changes in the ovarian and uterine arteries in women with PCOS has improved our understanding of the pathogenesis of this common condition and provides additional variables to the traditional endocrinological and more recent ultrasound features for its diagnosis (Kurjak, 1996). This technique has been used to study the hemodynamic changes in the uterine and/or ovarian arteries during menstrual cycle in women with normal ovaries (Battaglia *et al.*, 1995). It was also reported a higher uterine artery pulsatility index in women with PCOS and a decreased resistance index within the ovarian stroma in PCOS. This suggest that an increase in downstream resistance and a positive correlation with LH levels. The latter is associated with severe insulin resistance and hyperinsulinaemia and is an occasional finding in PCOS. Treatment of PCOS depends on the presentation of patients, desire for fertility and the need for contraception. Different approaches have been practiced; including non-medical, such

as weight loss (Polson, 1988), medical, such as using Metformin or spironolactone (Spritzer *et al.*, 2000) or clomiphene citrate and Metrodin (Wang *et al.*, 1980). Surgical approach has also been practiced that include ovarian wedge resection, laparoscopy methods (Stein, 1964). Complications; women suffering from PCOS are at risk for developing DM type 2, hypertension, intravascular thrombosis, coronary artery disease and endometrial cancer (Wild *et al.*, 2000).

Experimental section

Patients and Methods: This is a prospective study consisted of 50 female patients at the reproductive age. All patients attained the infertility clinic were seeking consultation either primary and/or secondary infertility. A complete history of each patient was recorded on especially prepared data sheets including; type of infertility, duration of infertility, age group (15-19, 20-24, 25-29, 30-34, 35-39 and > 40) in years, parity, gravity, menstrual abnormalities, amount of blood loss, duration of blood loss and duration of cycle. Each patient was examined as general and special gynecological examination with focus on the evidence of overt hirsutism, acne, obesity (body mass index, BMI), which is equal to weight(kg)/height (m), normal range between (Fox *et al.*, 1994; Conway, ?; Adams, 1996; Fleischer, 1997; Kurjak, 1996; Battaglia *et al.*, 1995; Polson *et al.*, 1988; Spritzer *et al.*, 1999; Wang *et al.*, 1980; Stein, 1964; Wild *et al.*, 2000), more than this was abnormal. All cases with suspicion of PCOS were directed to ultrasound unit for the evidence of typical polycystic ovaries, which are 10 or more peripheral poorly developed atretic follicles of a diameter between 2-10mm, in an enlarged ovary demonstrating stromal hypertrophy. The ovaries are obviously enlarged (> 6 cm³) and are usually twice normal size (2 x 2 x3 cm). The follicles, however, are smaller without evidence of a dominant follicle and the ovarian volume and stromal echogenicity are greater. Venous blood samples were taken at early follicular phase of menstrual cycle, the clotted blood was centrifuged and the drawn serum was used for RIA to estimate the concentration of LH and FSH levels. All data were collected and statistically analyzed.

RESULTS

The collected data and information of the present study from 50 cases have been analyzed and interpreted. The percentage of cycle abnormality was higher among all clinical features reaching 82%, while the percentage of infertility was 80%. Hirsutism, acne, and obesity were 60%, 40% and 26% respectively, as illustrated on (Table 1). The percentage of PCOS was more common in urban area reaching 70%, while, in the rural area it was 30%. The secondary infertility was 64%, while the primary infertility was 16%, as shown on (Table 2). Parameters of patients with PCOS (Table 3) were recorded to show higher percentage of PCOS occurs in age group (25-29) of 30%, because at this group the patients usually attending clinic for cycle abnormalities and infertility. Lower percentage in age groups (20-24), (35-39) and (> 40) were 12%. Moreover, the percentage at age groups (30-34) and (15-19) were 16% and 18% respectively. Irregular cycle was found in 76% of patients, while regular cycle was recorded in 24% of patients. Scanty blood loss was 66% of patients, and normal and excessive losses were 22% and 12% respectively. In 76% of patients, the duration of cycle (>35 days), and the cycle lasts (< 28 days) and between (28-35 days) in 12% of patients.

Box 1. Manifestation of PCOS at different ages

In utero	Peripuberty	Adolescence & Adulthood	Ageing
Small baby syndrome • Intrauterine growth retardation Lead to: Long-term health effects	Exaggerated adrenarche Increased levels of: • Adrenal androgens • Insulin Functional ovarian Hyperandrogenism Lead to: Precocious puberty	PCOS • An-ovulation • Hyperandrogenism • Polycystic ovaries • Obesity (50%) Lead to: Reproductive disorders	Metabolic syndrome • Diabetes • Hypertension • Dyslipidemia • Increased plasminogen activator inhibitor-1 Lead to: Metabolic effects

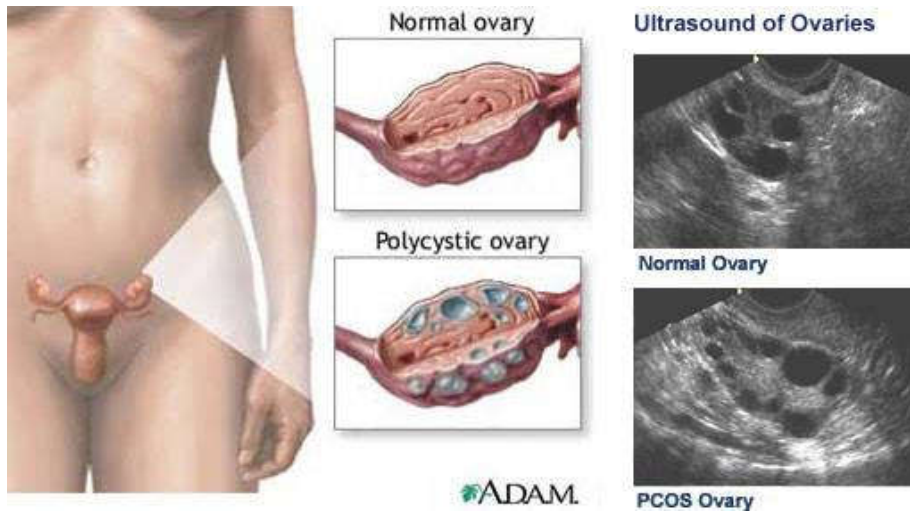


Figure 1. The difference between normal ovary and polycystic ovary

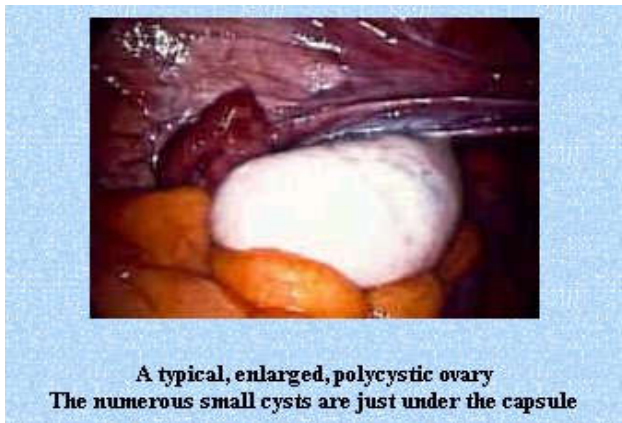
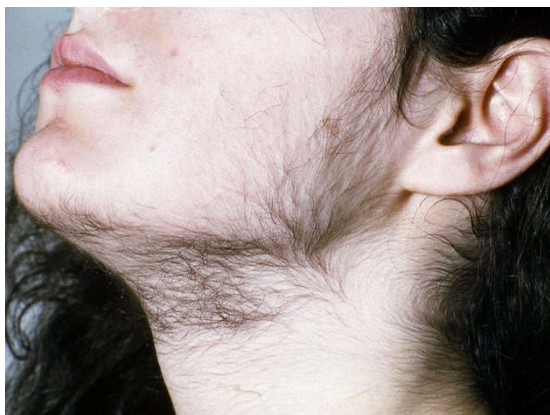


Figure (3A): Polycystic ovaries, showing increased size and a smooth white surface reflecting the thickening of the capsule.



Figure (3B): Section through polycystic ovary showing multiple cysts with diameter of <10 mm arranged around the periphery of the ovary. The stroma is increased and the ovary is enlarged



A:- Young woman with PCOS showing facial hirsutism



B:- Axillary acanthosis nigricans

Figure 4. Skin manifestation of PCOS

Table 1. The relationship between clinical features of PCOS and the percentage of incidence

Clinical feature	No. of patients %	Percentage of Incidence	P value
Acne	20 (40)	40	0.936
Cycle abnormality	41 (82)	82	0.000*
Hirsutism	30 (60)	60	0.936
Infertility	40 (80)	80	0.000*
Obesity	13 (26)	26	0.003

*Statistically significant differences at p< 0.05

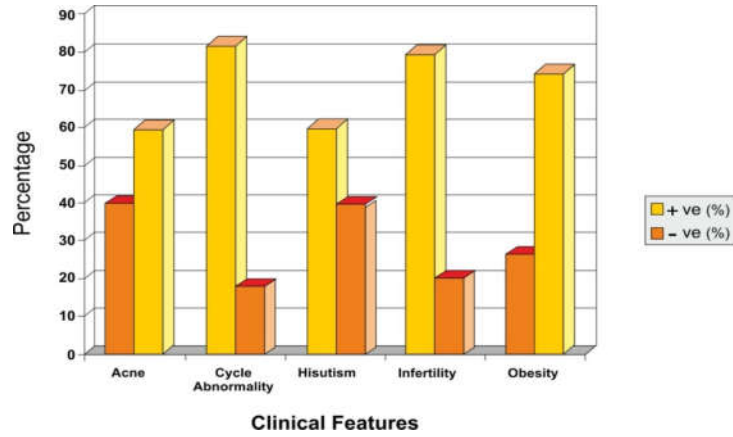


Table 2. Some parameters for patients with PCOS

Age group	No. of Patients	Residency		BMI	Infertility		Duration of Infertility		Parity in patients with secondary infertility
		Rural	Urban		primary	secondary	Primary	secondary	
15-19	9	3	6	26-32	2	6	1-5 3±2.8	3-6 3.5±1.2	1
20-24	6	1	5	25-30	1	4	2	3-6 4.5±1.2	1
25-29	15	5	10	23-31	2	12	1-8 4.5±4.9	2-6 4±1.3	1
30-34	8	3	5	26-31	1	5	2	3-6 4.5±2.1	P ₂
35-39	6	1	5	25-28	1	3	3	3-5 4±1.9	P ₂
>40	6	2	4	30	1	2	2	2-3 2.5±0.7	P ₂
Total	50	15 30%	35 70%	--	8 16%	32 64%			
P value		0.031*			0.041*				

* Statistically significant differences at p< 0.05

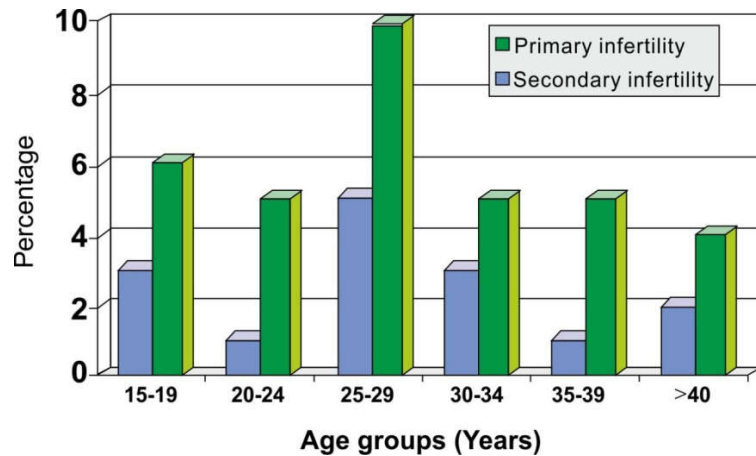


Table 3. Parameters of patients with PCOS

Age group	No. of patients	Cycle		Blood loss (Subjective)			Duration of cycle (days)			Duration of blood loss (days)		
		Regular	Irregular	Scanty	Normal	Excessive	< 28	28-35	> 35	< 5	5-7	> 7
15-19	9 (18%)	2	7	5	3	1	1	1	7	7	1	1
20-24	6 (12%)	2	4	4	1	1	1	1	1	4	1	1
25-29	15 (30%)	3	12	10	4	1	1	2	12	12	2	1
30-34	8 (16%)	2	6	6	1	1	1	1	6	6	1	1
35-39	6 (12%)	2	4	4	1	1	1	1	4	4	1	1
>40	6 (12%)	1	5	4	1	1	1	1	4	4	1	1
Total	50	12 24%	38 76%	33 66%	11 22%	6 12%	6 12%	6 12%	38 76%	38 76%	6 12%	6 12%
P value		0.024*		0.037*			0.003*			0.003*		

*Statistically significant association at p<0.05.

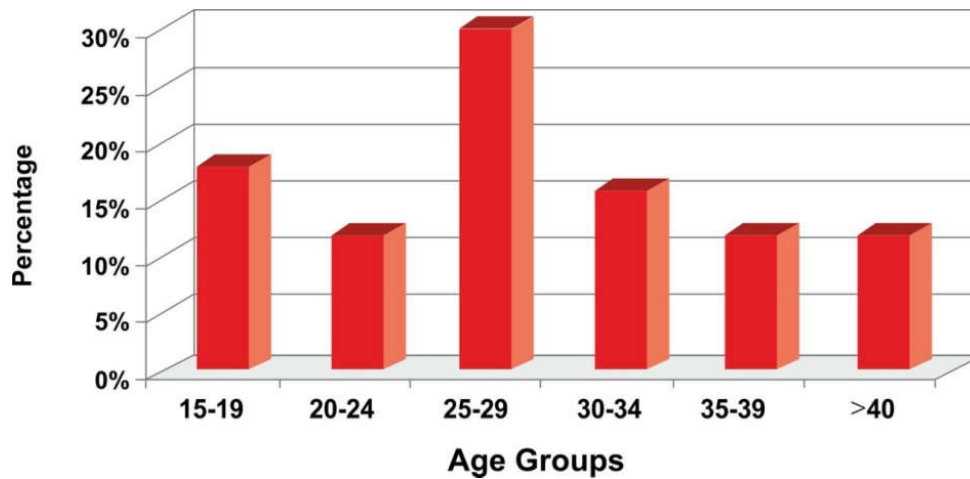


Table 4. Relationship between clinical features of PCOS and hormonal assay

Clinical Feature	LH				FSH	
	Mean ± SD	No. of Patients	Percentage %	P value	Mean ± SD	P value
Acne	19.47± 6.798	10	50	0.019*	6.411± 2.834	0.017*
Hirsutism	18.69± 7.131	15	50	0.024*	5.249± 3.254	0.031*
Menstrual cycle abnormality	23.21± 10.27	16	39.02	0.004*	8.303± 5.912	0.000*
Infertility	22.806±10.578	18	45	0.014*	3.9± 6.214	0.021*
Obesity	17.015± 6.316	7	53.8	0.033*	9.298±8.151	0.441*

* Significant differences at p< 0.05 (independent sample t-student test).

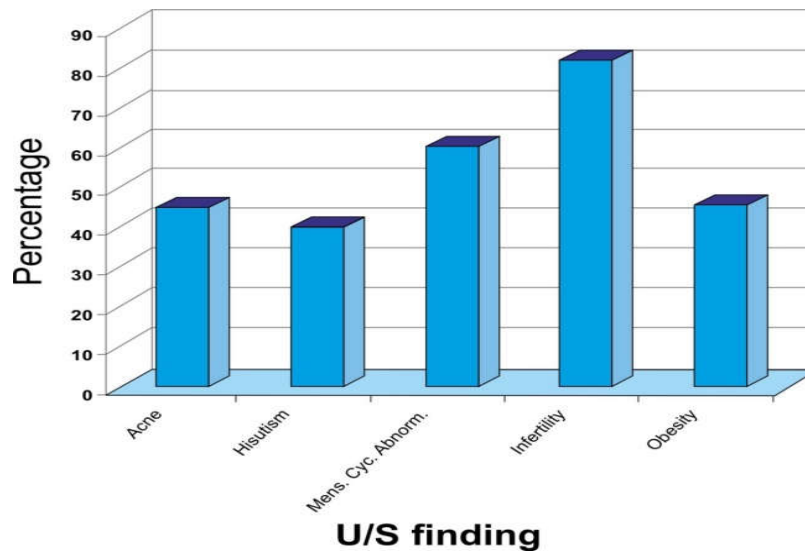


Table 5. The relationship between US findings of PCOS and clinical features

Clinical feature	No. of patients	US finding	Percentage	P value
Acne	20	9	45	0.137
Hirsutism	30	12	40	0.113
Menstrual cycle abnormality	41	25	60.9	0.043*
Infertility	40	33	82.5	0.002*
Obesity	13	6	46	0.136
Total	144	85	59	

*Significant differences at p < 0.05

Table 6. The relationship between US findings and LH and FSH results

US findings	No. of patients	LH	No. of patients	%	P value	FSH	P value
Ovarian size	33	13.5-39.7 26.06±8.474	20	60.6	0.013*	0.5-9 5.364±1.977	0.078
Stroma echogenicity	33	13.5-39.7 26.06±8.474	20	60.6	0.013*	0.5-9 5.364±1.977	0.078

*Significant differences at p < 0.05 (Independent sample t-student test).

Duration of blood loss lasts (< 5 days) in 76% of patients, while, it last between (5-7 days) and (>7 days) in 12%. The relationship between clinical features of PCOS and hormonal assay of LH and FSH was given on (Table 4), and as follows; The mean level of LH in patients with acne was (19.47), with hirsutism was (18.69), with cycle abnormalities was (3.21), with infertility was (22.80), and with obesity was (17.01). Moreover, the mean level of FSH in patients with acne was (6.41), with hirsutism was (5.24), with cycle abnormality was (8.30), with infertility was (8.30) and with obesity was (9.29). The present finding has shown that patients with obesity had high level of LH (53.8%), as compared to other clinical features, whereas, the levels of LH has increased in patient with acne and hirsutism (50%). Patients with infertility has recorded level of LH as (45%) and with menstrual cycle abnormality as (39.02%). An FSH level was normal in all patients. The percentage of ultrasound finding, which is more common in patients with infertility was (82.5%), while, in patients with menstrual cycle abnormality was (60.9%) and in obese patients (46%) and in patients with acne was (45%) and in patients with hirsutism was (40%), as outlined on (Table 5). The relationship between ultrasound finding with respect to LH and FSH levels (Table 6), was as follows; the mean level of LH and FSH were (26.06) and (5.36) respectively. This study has showed an increased level of LH (60.6%) in patients with increase in ovarian size and stromal echogenicity. FSH level was normal.

Percentage of PCOS more common in Urban area was (70%), while in rural area was (30%) and secondary infertility (64%) higher than primary (16%). Higher percentages of PCOS occur in age group between (25-29) and were 30%. However, lower percentages in age group of (20-24), (35-39), (> 40) were 12%. While, age groups of (30-34) and (15-19) were 16% and 18% respectively. Irregular cycle was found in 76% of patients, while regular cycle was in 24%. Scanty blood loss was in 66% normal and excessive loss was 22% and 12% respectively. In 76% of patients, the duration of cycle (> 35 days), and cycle lasts (> 28 days) and between 28-35 days in 12% of patients. Duration of blood loss last (< 5 days) in 76% of patients, while, it lasts between (5-7 days) in (12%), as listed on (Table 3). These results are statistically significant and comply with the previous results of Zoe, et.al (1998). Clinical features of PCOS and hormonal changes with respect to LH and FSH, the study has shown that patients suffering obesity had high level of LH (53.8%), as compared to other clinical features. which is statistically significant (Table 4). Whereas, the level of LH has increased in patients with acne and hirsutism to (50%), which are statistically significant. Patients with infertility have level of LH around (45%) and menstrual cycle abnormality was (39.02%), which is statistically significant. FSH level was normal in all patients, which is statistically significant. These results comply with the previously reported results by Pasquali *et al.* (1989).

The clinical features of PCOS related to ultrasound findings (Table 5) have indicated high percentage in patients with infertility (82.5), which is statistically significant. While, in patients with menstrual cycle abnormality was (60.9%), which is statistically significant. However, in obese patients it was (46%), and in patients with acne was (45%) and in patients with Hirsutism was (40%). These results comply with the findings of Dewaily *et al* (1997). Meanwhile, the ultrasound findings revealed that the levels of LH and FSH have indicated that there was an increase in the level of LH (60.6%) in

patients with increase ovarian size and increase stromal echogenicity, which is statistically significant, while, it was found that normal level of FSH was recorded (Table 6). These results comply with the finding of Conway *et al.* (1992) The study showed an increased level of LH (60.6%) in patients with increased ovarian size and an increase stromal echogenicity, while normal FSH level.

DISCUSSION

PCOS is the most common form of an-ovulatory infertility, which is characterized by a particular ovarian morphology and associated with menstrual disturbance and alter hormonal parameters. Criteria of the US National Institutes of Health Polycystic ovarian syndrome include; presence of menstrual abnormalities and an-ovulation; presence of clinical and /or biochemical hyperandrogenaemia; absence of hyperprolactinemia or thyroid disease; absence of late-onset congenital adrenal hyperplasia and absence of Cushing's syndrome. Polycystic ovaries are characterized by the following parameters: presence of polycystic ovaries on ultrasound examination; absence of menstrual or cosmetic symptoms and absence of biochemical hyperandrogenaemia. Moreover, the Idiopathic hirsutism is characterized by the following clinical cases: presence of excess hair growth and absence of biochemical hyperandrogenaemia. The result of the present study showed that 40% of patients with PCOS have acne (Table 1).

This result corroborates with the previous finding reported by Daniel *et al* (1997), which reported approximately 35% of patients have acne. Whereas, the hirsutism was 60%, which comply with Daniels *et al* study (66%). This variation could be contributed to other causes of Hirsutism. Moreover, it was found that the percentage of obesity was 26%, as compared with Daniel *et al.* (1997) (28%), and this is statistically significant. Our finding (Table 1) regarding infertility problem was 80% and the result was consistent with Daniel *et al.* (1997) and the result is statistically significant. The present study showed higher incidence of PCOS in urban areas (70%). This may be due to the lifestyle of patients living there, while, in rural areas (30%), which is statistically insignificant. The present study showed higher percentage of secondary infertility (64%) than primary (16%), which is statistically significant (Table 2). These results comply with Dunaif *et al* (9) findings. The relationship between the age group and PCOS has indicated higher incidence occur at (25-29), which was 30%, because at this age, patients usually attend clinic for cycle abnormalities and infertility (Table 3). This investigation has showed irregular cycle in 76% of patients, while, regular cycle in 24% of patients, which is statistically significant. The present finding showed that scanty blood loss was estimated in subjectively 66% of patients, while, normal and excessive blood loss were 22% and 12% respectively, which is statistically significant. However, the duration of the cycle lasts (> 35 days) in 76% of patients with duration of blood loss (< 5 days), while, the cycle lasts (< 28 days), and between (28-35 days) with duration of blood loss (5-7 days) and (> 7 days) occur in 12%. These results are statistically significant and comply with Zoe *et al.* (1998).

Conclusion

In patients with PCOS, it is concluded that there is a direct relationship and the biochemical investigations and the

increase in ovarian size and stromal echogenicity. PCOS is presented with secondary infertility (64%), while, in primary infertility it was only (16%). PCOS was more common in urban areas and recorded (70%), while in the rural area it was (30%). The use of ultrasound is more accurate than the biochemical investigations in the diagnosis of PCOS.

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