

## Endocrine Disturbances in Polycystic Ovary Syndrome

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### ABSTRACT:-

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder of unknown aetiology affecting 5-10% of women of reproductive age. It is a disorder that affects the reproductive, endocrine and metabolic systems, and it is the most common cause of anovulatory infertility. The purpose of this study is to investigate the endocrine disturbance in PCO. Two hundred infertile women attended Infertility Unit in Kirkuk were subjected to this study. Their ages range between 17 and 47 years ( $30.5 \pm 6.89$ ) with average duration of infertility at the time of the study was ( $7.23 \text{ year} \pm 4.60$ ). Twenty volunteer healthy fertile women of same age range as subjected infertile patients, with no clinical evidence of endocrine abnormalities were subjected to the study as a control group. The immunoradiometric assay of the follicle stimulating hormone (FSH), luteinizing hormone (LH), LH: FSH ratio, prolactin and progesterone hormones were carried out on samples obtained from each individual. Regarding the endocrinal evaluation in PCOS cases, our results revealed that mean values of serum LH, FSH and prolactin levels were significantly ( $P < 0.05$ ) elevated in most women who showed PCO and they reached  $35.79 \text{ IU/L} \pm 5.366$ ,  $15.89 \text{ IU/L} \pm 4.228$  and  $21.84 \text{ ng/L} \pm 9.534$ . LH:FSH ratio also showed a significant ( $p < 0.05$ ) increase in this group when compared with that of control group and reached  $2.49 \pm 1.12$  in infertile women with PCO. Mean value of serum progesterone level was significantly decreased in those women and declined to  $0.14 \text{ ng/L} \pm 0.214$ . Regarding the age of women, most cases of PCOS were at age groups 20-29 and 30-39 years which comprised 44.87 % of the 156 cases.

### الأضطرابات الغدية الصموية في متلازمة متعدد الكيسات في المبيض

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المستخلص:-

تعد متلازمة متعدد الكيسات في المبيض من الأسباب المهمة للعقم في النساء، حيث تصيب 5-10% منهن في عمر الأنجاب مؤثرة على الأنجاب وجهازي الأيض والغدد الصماء. يهدف البحث بيان الاضطرابات التي تحدث في بعض الغدد الصماء في حالات متلازمة متعدد الكيسات في المبيض من خلال قياس مستويات هورمونات البروجسترون Progesterone، البرولكتين Prolactin، هورمون المحفز للجري FSH وهورمون LH مع نسبة LH:FSH. خضعت للبحث منتي مريضة يعانين من العقم واللاتي يراجعن وحدة العقم في محافظة كركوك. تراوح أعمارهن ما بين 17-47 سنة مع معدل فترة العقم 7.23 سنة حين إجراء البحث. كما تم ادخال عشرين متطوعة سليمة من اللواتي لم تظهر عليهن اية أعراض يعزى الى اضطرابات في الغدد الصماء لأعتبارهن مجموعة سيطرة. تم قياس مستويات الهورمونات LH,FSH,Prolactin, Progesterone مع نسبة LH:FSH في نماذج دم الخاضعات للبحث كافة. ادلت النتائج بأن متوسط القيم لمستويات هورمونات LH,FSH,Prolactin قد أظهرت ارتفاعاً مهماً احصائياً ( $P < 0.05$ ) في النساء المرضيات حيث بلغت  $35.79 \text{ IU/L} \pm 5.366$  و  $15.89 \text{ IU/L} \pm 4.228$  او  $21.84 \text{ ng/L} \pm 9.534$  بالتعاقب بالإضافة الى زيادة في نسبة LH:FSH عند مقارنتها مع مجموعة السيطرة. أما مستويات هورمون البروجسترون فقد أظهرت نقصاناً مهماً احصائياً ( $P < 0.05$ ) في النساء المرضيات حيث نقصت الى  $0.14 \text{ ng/L} \pm 0.214$ . أما بالنسبة لأعمار النساء فقد وجد أن معظم حالات متلازمة متعدد الكيسات في المبيض كانت في مجموعة الأعمار 20-29 سنة و 30-39 سنة حيث شكلت نسبة 44.87% من الحالات.

## **INTRODUCTION:-**

Over the >60 years since Polycystic ovary syndrome (PCOS) was first recognized as a common entity, clinicians have entertained the notion that PCOS is a genetic disease [1-2]. PCOS is a heterogeneous disorder of unknown aetiology affecting 5-10% of women of reproductive age. It is a disorder that affects the reproductive, endocrine and metabolic systems, and it is the most common cause of anovulatory infertility. Its exact cause is unknown; however, there are several theories about its pathophysiology [3-4]. Infertility due to PCOS is a major problem worldwide (5). It is also one of reproductive problems in Iraq and is a subject of research among demographers [6].

However, although a large body of information is now available, the exact mechanisms underlying the reproductive dysfunction are still not clearly understood. Yet there is little on the prevalence, causes and treatments for PCOS among women from general population. The purpose of this study is to elucidate the prevalence of PCOS among women in Kirkuk province and investigate the endocrinal causes of infertility. To achieve that purpose, this study is designed and it aims at: (i) Clinical evaluation of women according to the criteria, (ii) Endocrine evaluations: Hormonal analyses of gonadotropin hormones (folicle stimulating hormone, leutinizing hormone and prolactin) and progesterone and (iii) Transvaginal sonographic examination of ovarian morphology.

## **PATIENTS AND METHODS:-**

**Patients:** Two hundred infertile women attended infertility unit in Kirkuk were subjected to this study. Their ages range between 17 and 47 years ( $30.5 \pm 6.89$ ) with average duration of infertility at the time of the study was ( $7.23 \text{ year} \pm 4.60$ ). All subjects underwent clinical screening included age, previous abortion, contraception, duration of infertility, and history (primary vs. secondary) of infertility; menstrual cycle history; any other previous medication and /or surgery. All infertile women presented with infertility were subjected to special criteria: (1) stopped any medication at least for three months before investigation. (2) They were infertile at

least one year (3) they had not been referred for *in vitro* fertilization (IVF) or intrauterine insemination (4) the spermograms of their husbands had been reported as normal and had no any reproductive disorders.

**Control:** Twenty volunteer healthy fertile women of same age range as subjected infertile patients, with no clinical evidence of endocrine abnormalities were subjected to the study as a control group.

**Sera Collection:** Blood samples were collected from antecubital vein into anticoagulant-free containers and allowed for clotting. Following centrifugation, sera were separated and stored at  $-20^\circ\text{C}$  until hormonal assessment.

**Hormonal Assay:** The immunoradiometric assay of the follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin and progesterone hormones was carried out according to the procedures prepared by Kits (IMMUNOTECH-A BECKMAN COULTER COMPANY) and processed on Gamma counter -Iso data- instrument (Block Scientific Inc.)

**Transvaginal Sonography: (TVS)** Transvaginal sonography of ovarian morphology was performed in all patients to search for ultra sonographic signs of polycystic ovaries applying the criteria published by Ardeans *et al.*[7] included assessment of the ovarian stroma, ovarian size and number and subcapsular cyst. The sonographic examinations were performed with (Medison- 3200).

**Analysis of the Data:** The clinical and biochemical data were documented and entered into the excel program. The results of laboratory tests in the study and control groups were compared using Student's t-test. All reported values are given as mean  $\pm$  SD and  $P < 0.05$  was regarded as significant.

## **RESULTS:-**

Of 200 infertile subjected women, only 158 women were diagnosed as infertile due to polycystic ovary. 129 of them were primary infertility and 29 of them were secondary (table-1). Miscarriage comprised 4.4% of cases. Regarding age-related cases, it very obvious from the same table that most of cases were at age groups 20-29 and 30-39 and comprised 44.94% and 44.30% respectively.

Regarding the endocrinal evaluation in PCOS cases, our results revealed that mean values of serum LH, FSH and prolactin levels were significantly ( $P < 0.05$ ) elevated in most women who showed PCO and they reached  $35.79 \text{ IU/L} \pm 5.366$ ,  $15.89 \text{ IU/L} \pm 4.228$  and  $21.84 \text{ ng/L} \pm 9.534$ . LH:FSH ratio also showed a significant ( $p < 0.05$ ) increase in this group when compared with that of control group and reached  $2.49 \pm 1.12$  in infertile women with PCO. Mean value of serum progesterone level was significantly decreased in those women and declined to  $0.14 \text{ ng/L} \pm 0.214$  (table 2). As shown in figure-1 most cases of PCOS were at age groups 20-29 and 30-39 years which comprised 44.87 % of the 156 cases. The PCOS group had PCO on ultrasound examination and had any of the typical clinical features (anovulatory menstrual cycles and/or oligomenorrhea, hirsutism, acne, and obesity) and/or biochemical features (elevated serum LH and / or decreased progesterone).

#### **DISCUSSIONS:-**

Ovarian function in infertile women with PCOS is characterized by disordered folliculogenesis and abnormal steroidogenesis, which are interlinked. PCOS comprised (32.57)% from the total cases of infertility and the diagnoses depended on the principle features of PCOS and presence of an ultrasound appearance with endocrinal features including anovulatory infertility, menstrual irregularity, elevated LH raised LH : FSH ratio. Many studies have focused on the association between miscarriage and recurrent spontaneous abortion and luteal phase defects, based on decreased progesterone concentration [8] or irregular menstrual cycle [9-10] amenorrhea [11] and PCO [12]. It was suggested that miscarriage occurred in women with PCOS because of the hypersecretion of luteinizing hormone (LH). This study showed some infertile women with

a history of miscarriage due to irregular menstrual cycle, PCOS and decreased serum progesterone.

Increased frequencies of hyperprolactinaemia [13] and of hypersecretion of LH [14] have been reported in women with miscarriage. The diagnosis of PCOS has been based on the symptoms of menstrual dysfunction, hyperandrogenism manifested as hirsutism and acne, obesity and anovular infertility; biochemical markers such as circulating gonadotropin levels; or the ultrasound image of the ovaries [15]. Wijeyaratne *et al.* [16] reported that the prevalence of PCOS may be higher in South Asian immigrants in Britain to be 52% with majority of them presenting with menstrual abnormality. In this study, infertile cases with PCOS comprised (34.36%) of total infertility cases with 86.54 % of them were with irregular menstrual cycle. A diagnosis of PCO is likely if there is a history of menstrual disturbance features of PCOS, in association with elevated LH [17]. The LH level provides much the same information the FSH level does. Another useful test is the LH:FSH ratio which is normally 1:1. If, however, the LH level is much higher than FSH level, this suggests a diagnosis of polycystic ovarian disease [18]. These findings document our results which revealed significant ( $p < 0.05$ ) elevation of both LH and LH/FSH ratio in PCO cases. The PCOS is associated with tonic hypersecretion of LH during the follicular phase of the cycle, and this might adversely affect both fertility and pregnancy outcome. Hypersecretion of LH might be secondary to elevated oestrogen levels found in PCOS or it might be a consequence of abnormalities in LH pulse amplitude and frequency [14, 19]. It is obvious from the results of present study, that there were significant ( $P < 0.05$ ) differences between measured hormones in women with PCOS and control group.

Table (1) Distribution of PCOS Cases According to the Age, Type of Infertility, Cycle Regularity and Miscarriage

Age groups	No. of cases	Percent age %	Type of infertility	Cycle regularity	Tubal patency	Abortion
17-19	7	4.43	Primary 7 Secondary -	Primary 2 Secondary -	Patent 7 Closed -	-
20-29	71	44.94	Primary 58 Secondary 12	Primary 6 Secondary 3	Patent 70 Closed 1(Lt )	3
30-39	70	44.30	Primary 55 Secondary 14	Primary 7 Secondary 1	Patent 70 Closed -	4
40-49	10	6.33	Primary 7 Secondary 3	Primary 2 Secondary -	Patent 9 Closed 1	-
Total	158	100	158	21	158	7

Table (2) Subjects Demographics

Characteristics	Normal (control) (n=24)	PCOS (n=156)
Age (years)	28.6 ± 7.34	29 ± 6.2
Duration of infertility (years)	-	6 ± 3
FSH (IU/L)	7.90 ± 2.965	15.891 ± 4.228 *
LH (IU/L)	7.54 ± 4.553	35.796 ± 5.366 *
Progesterone (ng/L)	8.51 ± 5.641	0.14 ± 0.214 *
Prolactin (ng/L)	14.52 ± 5.049	21.84 ± 9.534 *
LH to FSH ratio	0.99 ± 0.583	2.49 ± 1.12 *

\* P < 0.05

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