

## Studying the Effect of LeutiniZing Hormone and Follicular Stimulating Hormone on Poly Cystic Ovary Syndrome in Married and in Non-married Women

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### Abstract:

Polycystic ovary syndrome (PCOS) is a common disorder in female during reproductive age. The aim of this study was to find out the correlation between LH, FSH hormone and LH: FSH ratio and polycystic ovary syndrome .

The present study included 50 patients of polycystic ovary syndrome (25 married in age group ranged between 20-45 years and 25 unmarried women with age ranged between 15-18years) and a control group comprising of 30 women (15 married & 15 unmarried) in the same age. Blood samples were aspirated from individual from 2<sup>nd</sup> – 5<sup>th</sup> day menstrual cycle (early follicular phase) for those of normal cycle while for patients with Polycystic ovary syndrome blood sample were collected regardless to the duration of the cycle to measure FSH, LH, and LH:FSH ratio by using ELISA methods

The results of this study showed the mean levels of LH and LH/FSH ratio significantly elevated in PCOS groups compared with normal groups in both married and unmarried women. We suggested that changes in the LH level and LH: FSH ratio has a role in polycystic ovarian syndrome.

**Key words:** Luteinizing hormone (LH), Follicular Stimulating Hormones (FSH), polycystic ovary syndrome (PCOS).

### الخلاصة:

تعد متلازمة التكييس المبيضي واحدة من الامراض الشائعة بين النساء في سن الانجاب والتي تخضع لسيطرة الهرمونات الانثوية، ولأيجاد العلاقة بين هرموني LH وFSH والنسبة بين LH الى FSH مع متلازمة التكييس المبيضي شملت الدراسة 50 من المريضات المصابات بالمتلازمة قسموا الى مجموعتين ن 1 تحتوي على 25 مريضة متزوجة مصابة بمتلازمة التكييس المبيضي ذات فئة عمرية تتراوح بين 25-45 سنة ون 2 غير متزوجات ذات فئة عمرية تتراوح بين 15-18 سنة. بالإضافة الى 30 امرأة انظموا للدراسة كمجموعة سيطرة بواقع 15 امراه لكل مجموعة.

تم فحص عينات الدم من نساء مجموعة السيطرة عند اليوم الخامس من الدورة الشهرية (الطور الجريبي المبكر) بينما جمعت عينات الدم من النساء المصابات بمتلازمة التكييس المبيضي بغض النظر عن موعد معين من الدورة الشهرية. تم قياس هرموني LH و FSH والنسبة بينهما بطريقة الايلايزا، حيث اظهرت نتائج الدراسة ارتفاعا معنويا في معدل هرمون LH والنسبة بين LH الى FSH عند النساء المصابات بالتكييس المبيضي لكلا المجموعتين بالمقارنة مع مجموعتي السيطرة، كما لوحظ ارتفاعا معنويا عاليا لهرمون LH عند المقارنة بين المجموع الكلي للنساء المصابات ومجموعة السيطرة.

نستنتج من هذه الدراسة بأن التغيرات في مستوى LH والنسبة بين LH الى FSH لها دور مهم في حصول متلازمة التكييس المبيضي سواء كانت المرأة متزوجة ام غير متزوجة.

### Introduction:

Polycystic ovary syndrome (PCOS) is a common heterogeneous endocrine-logical disorder that occurs in 5% to 10% of women in reproductive age group. It is the most prevalent endocrine opathy and common cause of infertility [1]. Polycystic ovary syndrome consist of chronic anovulatio menstrual disturbance, hyper-

androgenism, polycystic ovary and meta-bolic syndrome [2,3,4].

Polycystic ovarian syndrome originally described in 1935 by Stein and Eventual. Typical endocrinological disturbances of this syndrome are often connected to Insulin Resistance (IR) and its consequences, Impaired Glucose Tolerance (IGT) or type 2 diabetes [5,6].

According to the majority of previous studies [7,8,9], IR or its reciprocal value Insulin Sensitivity (IS) could be an intrinsic defect in PCOS. Some authors have found defective insulin secretion [10,11,12]. Whereas others have described an increase of insulin secretion [13,14]. The typical features of a patient with PCOS are oligoamenorrhoea, Hyperandrogenism, anovulatory sub fertility obesity [15] and pregnancy losses [16]. However, a diagnosis of PCOS not based on ultrasound alone because multiple cysts in the ovaries are not present in all women, and cysts can be present in normal ovaries [17].

Blood tests can provide a more definitive diagnosis of PCOS including LH, FSH, total testosterone and prolactin [18]. The ratio of circulating levels of hormones (LH and FSH hormones) in polycystic ovary syndrome of both married and unmarried women.

The aim of the current study was to find the correlation between the levels of some hormones (LH and FSH hormones) in polycystic ovary syndrome of both married and unmarried women.

### **Material and Methods:**

The present study involved fifty infertile Iraqi women with age ranged between (15-45) years with polycystic ovary syndrome diagnosed by ultrasound examination at Al-Elwya Teaching Hospital/ Baghdad, during the period of time between May 2012 to October 2012. The samples of patients were divided into two groups, 25 (N<sub>1</sub>) married women, aged (20-45) years and 25(N<sub>2</sub>) unmarried women aged (15-18) years, which was compared with control groups (30 healthy women, 15 married and 15 unmarried).

Ten ml of blood samples were separated during 2<sup>nd</sup>-5<sup>th</sup> day of the menstrual cycle (early follicular phase) for those of normal cycle while for patients with polycystic ovarian syndrome. Samples were collected regardless to the duration of the cycle, the samples collected

into tubes and centrifuged within 30 minutes at 3000 RPM. Serum hormones measured using the Kit (Monobind Inc. Lake Forest, CA. USA) for follicle stimulating hormone product code: 425-300 [19] and (Monobind Inc. Lake Forest, CA. USA) for luteinizing hormone code:625-300 [21]. Both hormones (Luteinizing hormone (LH) and Follicular stimulating hormone (FSH) and LH: FSH ratio were determined by using ELISA method. Luteinizing hormone to follicular stimulating hormone (LH/FSH ratio) is a controversial criterion for identifying a sub-group of infertile women with PCOS and abnormalities at the level of the hypothalamic-pituitary-ovarian axis [20].

### **Statistical analysis:**

Chi-square<sup>2</sup> the statistical analysis system [22] was used to detected the differences factors in the parameters and to make comparative between percentages in this study.

### **Results:**

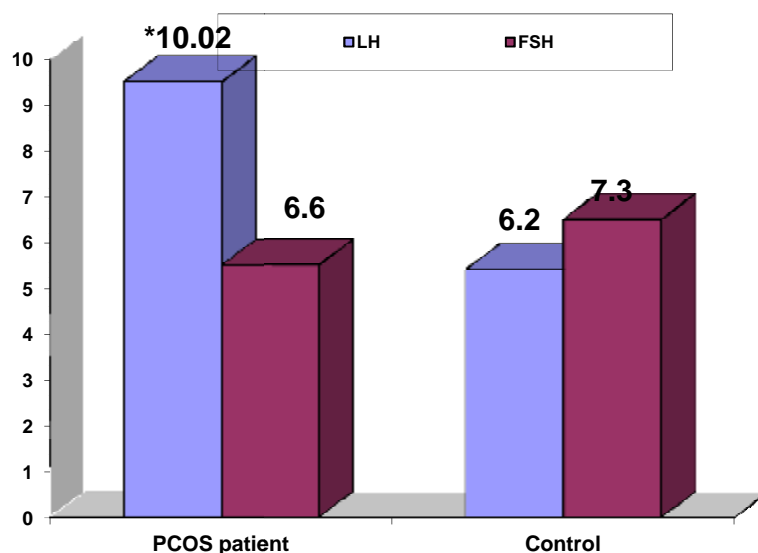
In this study the Mean serum level of LH and LH/FSH ratio were significantly (P < 0.005) elevated for PCOS patients, compared with control group (12.01± 0.10 mlU/ml), (6.91± 0.09mlU/ml) and (3.02±0.89 mlU/ml), (1.32±0.09 mlU/ml) respectively in group N<sub>1</sub> and (9.1 ± 0.7 mlU/ml), (5.01±0.14 mlU/ml) and (2.60±0.6 mlU/ml),( 0.98 ± 0.17 mlU/ml) respectively in group N<sub>2</sub>. FSH for PCOS patients were in the normal range with no significant difference at (P > 0.005) from control group as shown in table (1).

When we compared between the total PCOS patients and control group for LH and FSH, it was found that LH was significantly elevated for PCOS patients compared with control groups, whereas, FSH for PCOS patients were in the normal range with no significant difference from control group as shown in figure-1.

**Table -1: Levels of LH, FSH and LH/FSH ratio in (PCOS) patients and controls.**

Group description	No	LH ml.U/ml mean ± SD	P	FSH ml.U/ml mean ± SD	p	LH/FSH ratio mean ± SD	P
PCOS N1 (unmarried)	25	12.01 ± 0.10	<0.005*	6.12 ± 1.85	>0.005	3.02 ± 0.89	<0.005*
Control	15	6.91 ± 0.09	-	7.03 ± 1.94	-	1.32 ± 0.09	-
PCOS N2 (married)	25	9.1 ± 0.7	<0.005*	6.92 ± 1.70	>0.005	2.60 ± 0.6	<0.005*
Control	15	5.01 ± 0.14	-	7.05 ± 1.22	-	0.98 ± 0.17	-

\* Significant difference between PCOS patients and control group if P < 0.005.



**Figure-1: Comparison between the total PCOS patients (married and unmarried) and control group for LH and FSH.**

**Discussion:**

PCOS is associated with various endocrine abnormalities such as increased serum LH levels and increased ratio of LH: FSH [23]. Estimation of these hormones aids in the diagnosis. In PCOS ovary is enlarged >9 ml in volume, smooth, sclerotic, has thickened capsular & sub capsular follicular cysts with atresia and hyperplastic theca and stroma. Polycystic ovary contains 2-3 fold the normal number of follicles [24]. A classical ultrasound features of polycystic ovary syndrome described by Jonard *et al.* 2002 which included enlarged ovary with

presence of 10 or more cysts 2-8 mm in diameter arranged either peripherally “string of pearls “around dense core of stroma or scattered throughout an increased amount of stroma [25].

In the present study, PCOS patients had significantly elevated both LH level and LH: FSH ratio, for both married and unmarried groups when compared with controls (see table-1), this difference also showed between total patients with PCOS and control (see figure-1). Increased LH secretion with relatively fixed low or normal FSH secretion in women with PCOS was first

reported by Yen et al.<sup>[26]</sup>. Later studies showed an increase of both LH pulse frequency and amplitude, normal or low concentrations of FSH, an elevated LH:FSH ratio and increased LH responses to GnRH<sup>[27,28]</sup>. The ratio of LH to FSH varies; most pre-menopausal women have a ratio close to 1:1. In PCOS, the LH level may rise above the FSH significantly. Our results agree with recent study, who found the mean concentration of LH to be elevated in patients with PCOS and LH:FSH ratio was raised more in the unmarried group (56%) than in married group (26%), while (20%) of patients in the control group had an elevated LH:FSH ratio<sup>[29,30]</sup> recorded high LH:FSH ratio in (75%) of patients<sup>[31]</sup> and reported that 67.42% of their patients were having elevated ratio LH:FSH, while Ratio was significant and abnormally raised in 41% - 44% of patients in study of<sup>[32]</sup>.

Also Dipankar and Sharque<sup>[33],[34]</sup> found that LH:FSH ratio increased in 55.55% and 60% of patients respectively for patients were having raised LH:FSH ratio. In our study; the LH mean values were (10.02 mIU/ml) for total PCOS patients and (6.6 mIU/ml) for control as shown in the figure. LH mean values were found to be significantly elevated in patients group compared to controls ( $p < 0.005$ ). The explanation of normal LH in PCOS might be based on a typical PCOS in which LH level might be normal<sup>[35]</sup> or might be due to increase pulse frequency or episodic secretion of LH as reported previously<sup>[36,37]</sup>. Our study confirmed with<sup>[38]</sup> who concluded that LH elevated in 86.7% of patients.

Women with PCOS often have high levels of LH secretion that contribute to the high levels of androgens, and this along with low levels of FSH contributes to poor egg development and an inability to ovulate<sup>[39]</sup>. It has been suggested that changes in the LH level and LH:FSH ratio have a role in the pathogenesis of ovary<sup>[40]</sup>.

From the present study it has been suggested that changes in the LH level and LH:FSH ratio have a role in the pathogenesis and we can conclude the raised in LH was statistically significant in patients with PCOS. The raised in LH:FSH ratio in both married and unmarried women was also statistically significant.

### **Reference:**

- 1- Zargar, A. H.; Gupta V. K.; Wani, A. I.; Masood, S. R.; Bashir, M. I.; Laway, B. A.; Ganie, M. A. and Salahudin M. Prevalence of Ultrasonically Proved Polycystic Ovaries in North Indian Women with Type 2 Diabetes Mellitus. *Reproductive Biology & Endocrinology*. 2005. Vol. 3 (35). Pp: 362-67.
- 2- Dipankar, B.; Kumar, M. S.; Satinath, M. and Mamata, P. Clinical Correlation with Biochemical Status in Polycystic Ovary Syndrome. *Journal of Obstetrics & Gynecology of India*. 2005. Vol. 55 (1). Pp: 67-71.
- 3- Dabadgyhae, P.; Robert, B. J.; Wang, J.; Davis, M. J. and Norman, R. J. Glucose Tolerance Abnormalities in Australian Women with Polycystic Ovary Syndrome. *Medical Journal of Australia*. 2007. Vol. 187 (6). Pp: 328-331.
- 4- Jonard, S. and Dewailly, D. Follicular Excess in Polycystic Ovaries, Due to Intra Ovarian Hyperandrogenism May Be the Main Culprit for Follicular Arrest. *Human Reproduction Update*. 2004. Vol. 10 (2). Pp: 107-117.
- 5- Legro, R. S.; Kinselmann, A. R.; Dodson, W. C. and Dunaif, A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, Controlled study in 254 affected women. *clin. Endocrinol metab.* 1999. Vol. 84. Pp: 165-169.
- 6- Dunaif, A. Insulin resistance and the polycystic ovary syndrome: mecha-

- nism and implications for pathogenesis. *Endocr. Rev.* 1997. Vol. 18. Pp: 774-800.
- 7- Dunaif, A.; Segal, K. R.; Shelley, D. R. Green, G.; Dobrjansky, A. and Licholai, T. Evidence for distinctive and intrinsic defects in insulin action in polycystic ovary syndrome. *Diabetes.* 1992. Vol. 41. Pp: 1257-1266.
  - 8- Gennarelli, G.; Holte, J.; Berglund, L.; Berne, C.; Massobrio, M. and Lithell, H. Prediction models for insulin resistance in the polycystic ovary syndrome. *HuReprod.* 2000. Vol. 15. Pp: 2098 -2102
  - 9- Morin-Papunen, L. C.; Vauhkonen, I.; Koivunen, R. M.; Ruokonen, H. and Tapanainen, J. S. Insulin sensitivity, insulin secretion, and metabolic and hormonal parameters in healthy women and women with polycystic ovarian syndrome. *Hum Reprod.* 2000. Vol. 15. Pp: 1266-1274.
  - 10- O'Meara, N. M.; Blackman, J. D.; Ehrmann, D. A.; Barnes, R. B.; Haspan, J. B.; Rosenfield, R. L. and Polonsky, K. S. Defects in betacell function in functional ovarian hyperandrogenism. *J Clin Endocrinol Metab.* 1993. Vol. 76. Pp: 1241-1247.
  - 11- Ehrmann, D. A.; Sturis, J.; Byrne, M. M.; Karrison, T.; Rosenfield, R. L. and Polonsky, K. S. Insulin secretory defects in polycystic ovary syndrome: relationship to insulin sensitivity and family history of non-insulin-dependent diabetes mellitus. *J Clin Invest.* 1995. Vol. 96. Pp: 520-527.
  - 12- Ehrmann, D. A. Glucose intolerance in the polycystic ovary syndrome: role of the pancreatic beta-cell. *J pediatr Endocrinol. Metab.* 2000. Vol. 13. (7) Pp: 1299-1301.
  - 13- Holts, J. T.; Berne, C.; Wide, L. and Lithell, H. Restored insulin sensitivity but persistently increased early insulin secretion after weight loss in obese women with polycystic ovary syndrome. *J. Clin. Endocrinol. Metab.* 1995. Vol. 80 (5). Pp: 2586-2593.
  - 14- Holts, J.; Bergh, T.; Berne, C.; Berglund, L. and Lithell, H. Enhanced early insulin response to glucose in relation to insulin resistance in women with polycystic ovary syndrome and normal Annuals of Internal Medicine. 2000. Vol. 32 (8). Pp: 989-993.
  - 15- Steven, B. and Halls, M. D. Calculator and body weight comparison. May-2004. Pp: 122-124.
  - 16- Ehrmann, D. Glucose tolerance. *J Clin Endocrinol Metab.* 1994. Vol 78. Pp: 1052-1058.
  - 17- Myers, D. M. D. Inc. Objective Medical Information on obesity, weight Management, Eating Disorders, and Related Topics Appointments. 28 May 2004. Pp: 67-69.
  - 18- Velazquez, E. M.; Mendosa, S.; Hamer, T. and Sosa, F. C. J. Metformin therapy polycystic ovary syndrome reduces hyper insulinemia, insulin resistance and systolic blood pressure, while facilitating menstrual regularity and pregnancy. 1994. Vol. 43 (3). Pp: 647-655.
  - 19- Center for Research in Reproduction polycysticovary syndrome, University of Virginia, December 2004.14.
  - 20- Moran, C.; Garcia-Hernandez, E.; Barahona, E.; Gonzalez, S. and Bermudez, J. A. Relationship between insulin resistance and gonadotropin dissociation in obese and nonobese women with polycystic ovary syndrome. *Fertil Steril* 2003. Vol. 80 (4). Pp: 1466-72.
  - 21- Odell, W. D. and Parlow, A. F. J. *Clin. Invest.* 1981. Vol. 47 (15). Pp: 2551.
  - 22- Kosasa, T. S. Measurement of human luteinizing hormone. *Journal of reproductive medicine.* 1981. Vol. 26. Pp: 201-6.
  - 23- SAS. Statistical Analysis system, Users Guide. Statistical. Version 7<sup>th</sup>

- ed. SAS. Inst. Inc. Cary. N.C. USA. 2004.
- 24- Lobo, R. A. and Carmina, E. Importance of Diagnosing PCOS.
- 25- Jonard, S.; Robert, Y.; Cortet-Rudelli, C.; Pigny, P.; Decanter, C. and Dewailly, D. Ultrasound examination of polycystic ovaries: is it worth counting the follicles. *Oxford journal, medicine, human reproduction*. 2002. Vol. 18 (3). Pp: 598-603
- 26- Yen, S.; Vela, P. and Rankin, J. Inappropriate secretion of follicle-stimulating hormone and luteinizing hormone in Polycystic ovarian disease. *J. Clin. Endocrinol. Metab.* 1970. Vol. 30 Pp: 435-442.
- 27- Yen, S.; Jaffe, R. and Barbieri, R. Polycystic Ovary Syndrome (Hyper androgenic Chronic An ovulation) In *Reproductive Endocrinology. Physiology, pathophysiology and clinical management*. W. B. Saunders Company. 1999. Pp: 436-478.
- 28- Taylor, A. Polycystic ovary syndrome; *Endocrinol. Metab. Clin. N Am.* 1998. Vol. 27 (14). PP: 77-90.
- 29- Rahila, Y.; Musadiq, K.; Zeenat, K.; Shahnawaz, A. and Abdullah, W. L. Polycystic Ovarian Syndrome: Clinical Correlation with Biochemical Status. *Surgical Science*. 2012. Vol. 3. Pp: 245-248.
- 30- Nazir, F.; Sayeed, S.; Malik, M.; Aziz, H. and Rana, S. A. Polycystic Ovarian Syndrome—Diagnosis and Management in Fertility Deprivation. *Pakistan Journal of Obstetrics & Gynecology*. 1999. Vol. 12 (1-2). Pp: 59-71.
- 31- Adil, F.; Ansar, H. and Munir, A. A. Polycystic Ovarian Syndrome and Hyperinsulinemia. *Journal of Liaquat University of Medical and Health Sciences*. 2005. Vol. 4 (3). Pp: 89-93.
- 32- Lobo, R. A. and Carmina, E. Importance of Diagnosing PCOS.: *Annals of Internal Medicine*. 2000 .Vol. 32 (12). Pp: 989-993.
- 33- Dipankar, B.; Kumar, M. S.; Satinath, M. and Mamata, P. Clinical Correlation with Biochemical Status in Polycystic Ovary Syndrome. *J. of Obstetrics & Gynecology of India*. 2005. Vol. 55 (1). Pp: 67-71.
- 34- Sharquie, K. E.; Al-Bayatti, A.; Al-Bahar, A. J. and Al-Zaidi, Q. M. A. Acanthosis Nigricans as Skin Manifestation of Polycystic Ovary Syndrome in Primary Infertile Females. *Middle East Fertility Society Journal*. 2004. Vol. 9 (2). Pp: 136-139.
- 35- Berger, M. J.; Taymor, M. L. and Patton, W. C. Gonadotropin levels and secretory patterns in patients with typical and atypical polycystic ovarian disease. *Fertil. Steril.* 1975. Vol. 26 (5). Pp: 619-626.
- 36- Waldstreicher, J.; Santoro, N. F.; Hall J. E.; Filicori, M. and Crowley. W. F. Hyperfunction of the hypothalamic-pituitary axis in women with polycystic ovarian disease: indirect evidence for partial gonadotroph desensitization. *J in. Endocrinol. Metab.* 1988. Vol. 66 (1). Pp: 165-172.
- 37- Venturoli, S.; Porcu, E.; Fabbri, R.; Magrini, O.; Gammi, L.; Paradisi, R. and Bolzani, R. Episodic pulsatile secretion of FSH, LH, Prolactin, estradiol, oestosterone and LH circadian in PCOS; *Clin. Endocrinol.* 1988. Vol. 28 Pp : 93-107.
- 38- Nasr, A. A.; Hamzah, H.; El Maaty, Z. A.; Gaber, H. and Azzam, O. Transvaginal Appearances of Ovary in Infertile Women with Oligomenorrhoe. Association with Clin. & Endoc. Profile. *Middle East Fertility Society Journal*. 2004. Vol. 9 (2). Pp: 140-149.
- 39- Melek, E.; Inan, A.; Emre, B.; Okan, B.; Neslihan, T. and Nilgun, D. A new perspective in diagnosing polycystic ovary syndrome; *J. Natl. Med. Assoc.* 2007. Vol. 99 (2). Pp: 149-152 .
- 40- Meigs, J.; Wilson, P.; Fox, C.; Vasan, R.; Nathan, D.; Sullivan, L. and D'Agostino, R. Body mass index, metabolic syndrome, and risk of type 2 diabetes or cardiovascular disease; *J. Clin. Endocrinol. Metab.* 2006. Vol. 91 (4). Pp: 2906-2912.