

## Study of follistatin and sex hormones level in women with polycystic ovarian syndrome in Baghdad

Ikhlass Abdul wahab Maarouf , Zaid Mohamad Mubarak

Department of Biology, college of Science, University of Tikrit, Tikrit , Iraq

DOI: <http://dx.doi.org/10.25130/tjps.23.2018.061>

### ARTICLE INFO.

#### Article history:

-Received: 11 / 12 / 2017

-Accepted: 12 / 3 / 2018

-Available online: / / 2018

**Keywords:** PCOS, Follistatin.

Corresponding Author:

**Name:** Ikhlass Abdul wahab

**E-mail:** [ikhlasslab@gmail.com](mailto:ikhlasslab@gmail.com)

**Tel:**

### Abstract

The aim of this search was to study the levels of follistatin and a number of sex hormones of polycystic ovary syndrome patients (PCOS). The study included 70 blood samples of women infected with PCOS and 20 samples from healthy women as control. The study had been performed in Baghdad / Kamal al-Samarrai Hospital. The patient had been diagnosed with ultrasound waves (sonar device) by specialized physicians in the hospital. The research requirements for the period from September 2016 to March 2017. The results showed high significant difference ( $p < 0.01$ ) in the concentration of follistatin in women with PCOS compared with healthy women. On the other hand, there was a significant decrease ( $p < 0.01$ ) in the concentration of follicle stimulating hormone (FSH) in women with PCOS compared to control. The results showed high significant increase ( $P < 0.01$ ) in the concentrations of prolactin hormone and testosterone hormone in patients with PCOS compared to control.

### Introduction

Polycystic Ovarian Syndrome (PCOS) is one of the most common endocrine disorders in women during childbearing age [1] and it's a common cause of lack of ovulation and infertility [2]. This syndrome is responsible for more than 53% of cases of infertility resulting from non-ovulation [3]. Women with PCOS follistatin were increases [4] or in patients with type 2 diabetes [5]. Follistatin is a protein that is able to bind and neutralize the actions of many body organs and it's plays a role in suppressing FSH secretion and activin A [6]. Also, the proportion of prolactin increases in most cases of polycystic ovaries, while the low rates of prolactin are obtained at menopause and increase in the cases of liver disease and kidney failure and tumors that affect the secretion cells of the prolactin [7,8]. Prolactin hormone that affects reproduction and sexual contact [9]. The amount of testosterone hormone in females, usually low and this amount is mostly from the process of transfiguration of Androstanedione which produced by the ovary and adrenalin to the testosterone and get this transfiguration outside the ovarian tissue, and notes that the male hormone in females has two images a small part of it is free, the active part of this hormone and the largest part is found in combination with the compound is the inactive part [10]. This study aimed

to determine the concentration of follistatin and some sexual hormones in (PCOS) patients in Baghdad.

Material and methods:

#### A. Samples collection

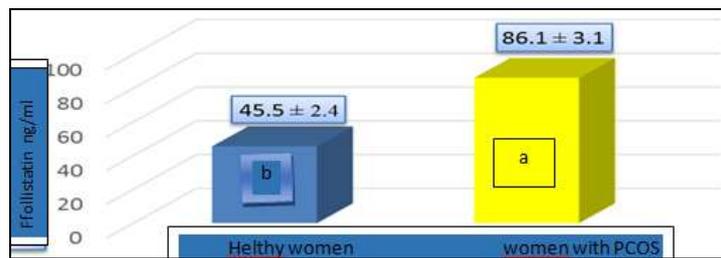
The study was conducted in Kamal Al-Samurai Hospital in Baghdad, Iraq for the period from September 2016 to March 2017. The study included about 70 women who had polycystic ovaries and ranged between (18-40) years after confirming their condition through clinical symptoms and clinical tests by specialized physicians. In addition to selecting control group of 20 women who are healthy women aged between (18-40) years, it was confirmed their safety from polycystic ovaries, infertility or any hormonal disorders or chronic diseases ., in addition to the tests blood samples were withdrawn from the women who were ill on the second day until the fourth day of the menstrual cycle.

B. The tests were carried out on patients' sera, included the follistatin concentration, which was supplied by the Shanghai Chinese company, and (prolactin, testosterone, FSH) hormones, which is equipped by Monobind Inc in America., and the tests were carried out according to the instructions of the processed company.

## Results and discussion

The results showed high significant increase ( $P < 0.01$ ) in follistatin concentration in patients with P.C.O.S

compared with the control women, as respectively ( $86.1 \pm 3.1$ ) and ( $45.4 \pm 2.4$ ) (**figure 1**).

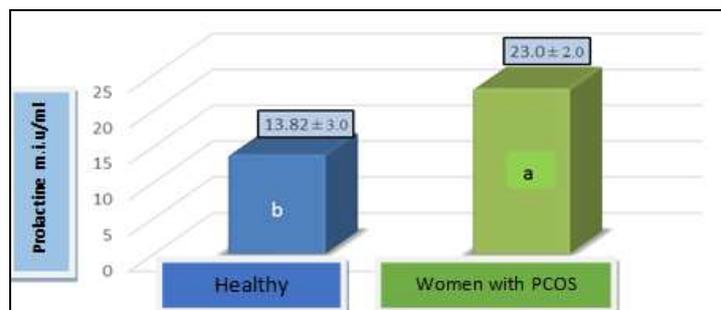


**Figure (1): Concentration of follistatin in women with PCOS and healthy women**

The results of the present study indicate that the concentration of follistatin in women with PCOS [11] compared to the control group may be related to the decrease in the concentration of Follicular stimulating hormones (FSH) because of an inverse relationship between the concentrations of the both hormones and this corresponds to the study [12,13]. These studies confirmed that follistatin leads to increased production of ovarian androgens and reduced FSH levels in the blood. In addition, the study [14] showed a significant increase in concentrations of the hormone Inhibin B and follistatin hormones in women with PCOS compared to women with control. Based on the results of the current study and other

studies that correspond to the results, we can conclude that ovarian cells possess an intrinsic property to release of high amounts of Inhibin B and follistatin PCOS patients compared to natural cells that do not possess this characteristic. In the study [15] the results showed that follistatin was a strong and influential marker in the functional side of both the reproductive and metabolic pathways associated with the cases experienced by the infected PCOS.

The results showed high significant increase ( $p < 0.01$ ) in the concentration of prolactin in patients with PCOS compared with the concentration of prolactin in healthy women (control), respectively ( $23.0 \pm 2.0$ ) and ( $13.82 \pm 3.0$ ) (figure 2).



**Figure (2): Concentration of prolactin in women with PCOS compared with healthy women**

The results of the present study indicate that the proportion of prolactin in the serum of women with PCOS compared to the control group and a significant level ( $P < 0.01$ ) this increase may be due to menstrual cycle disorders for women, causing their sterility through the effect of the hormone on the (FSH) and therefore causing a defect in the process of ovulation, and the study [16] indicate that the levels of prolactin are different during the menstrual cycle, where the concentration of the hormone in the second half of the menstrual cycle, while decreasing its concentration in the first half, specifically in the follicular phase, that was mentioned in study [17] and this study is deference with our study which shown us through the tests conducted a clear increase in the concentration of prolactin during the first phase of the vesicular phase, which was accompanied by the rise of the hormone follistatin in the same period of time and this confirms here that the hormone prolactin has close relationship with the hormone. The concentration of follistatin is associated with an

increase in prolactin in women with PCOS. The relationship between prolactin and follistatin may be positive and the concentration of these hormones increases, causing infertility of women, The reason for the return of high concentration of prolactin due to the use of drugs that increase the concentrations of the hormone in the blood, especially the following drugs (Phenothiazine, insulin, Haloperido, Isoniazid, sedatives) may increase the concentration of milk hormone from the normal level in patients with PCOS to increase the stimulation Lactotrophs, which is responsible for production in the anterior lobe of the pituitary gland, which may lead to increased secretion and its increase is always associated with the secretion of milk in women, which has been observed in some women with PCOS [18, 19]. That high concentration of the hormone causes menstrual disorders and causes infertility in women through the effect of the hormone prolactin on the (FSH) and thus its effect on the figureation of the egg in the early stages of its establishment, causing a defect in the

process of ovulation, and this is consistent with the study [20]. The high milk hormone correlates often positively with infertility, obesity, diabetes, and vice versa with male hormone [21]. The occurrence of any decrease in the concentration of prolactin is due to several different reasons, which include the excessive production of dopamine and serotonin. The high concentrations of prolactin hormone in women with PCOS may be the result of a previous pregnancy has

been shown to reach the concentration of hormone to 90% Immediately after birth and some women, there concentrations remain high because of their sterility [22].

The results showed a significant decrease in the concentration of FSH in the women who were infected with P.C.O.S compared to its concentration in healthy women (control) and respectively ( $6.84 \pm 1.21$ ) ( $8.19 \pm 1.62$ ) (figure 3).

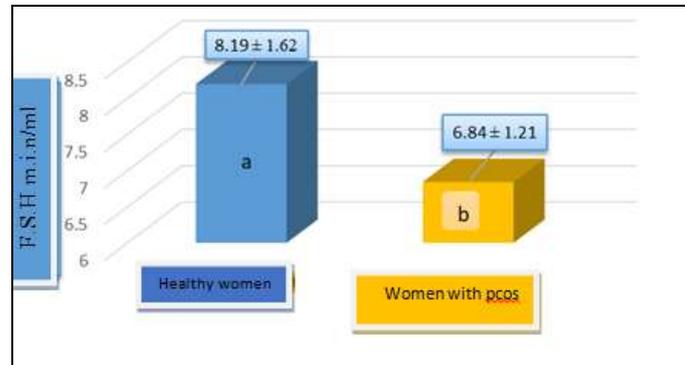


Figure (3): Concentration of FSH in infected women compared to control

The concentration of FSH in women with PCOS is lower than in healthy women (control) and these low concentrations of FSH indicate a defect in the secretion of follicle hormone. The lower hormone concentration, incidence of infertility in women. In this study, In polycystic ovaries, they had low concentrations of FSH, and this difference was due to a clear defect in the concentration of the hormone in women with PCOS, and this mention in study [23] which indicate that the reduction in the concentration of follicle stimulating hormone may be due to the adrenal gland, which produces adrenaline, which in turn affects the concentration of FSH through the secretion of androgens and estrogens. We believe that these low levels of hormone may be due to the mechanism of hormonal restraining of FSH by the mechanism of feedback negative feedback, and this corresponds to the results of the study [24]. That any decline in the concentration of FSH is due to the process of inhibiting the action of this hormone mediated by the prolactin and this is shown in this study through tests perfigured on patients as well as the high concentration of prolactin hormone inhibits

the secretion of FSH hormone, and that was mention in study [25], that prolactin concentrations of women with polycystic ovaries increased with decreased FSH concentrations. Since the hormone is one of the dominant factors in the figureation of the egg, any imbalance in the concentration of the hormone causes delayed pregnancy. The low blood levels of the hormone act as a strong stimulant to increase the secretion of follistatin, which inhibits the action of FSH in the early stages of the follicular phase, affecting the figureation of the egg and thus the occurrence of polycystic ovarian. This study agrees that the follistatin increases its concentration when the concentration of FSH has been detected and found that the levels of follistatin is significantly higher in patients with PCOS, regardless of obesity and this is confirmed by the study [26].

The results showed high sighnificant increase ( $P < 0.01$ ) in concentration of testosterone in patients with P.C.O.S compared with the concentration in healthy women (control), respectively ( $0.73 \pm 0.250$ ) and ( $0.485 \pm 0.160$ ) (figure 4).



Figure (4):The concentration of testosterone in the serum of women with PCOS compared to healthy women

In this study, the concentration of testosterone hormone in women with PCOS was higher than that of healthy women. Polycystic ovarian syndrome is a common cause of the high incidence of male hormone and hair density with obesity, and this is confirmed by the study [27] and increased susceptibility to type 2 diabetes [28], the incidence of this case is 50% of patients with PCOS and obesity is clear around the waist and increase the risk of cardiovascular disease and diabetes in the future, where these results indicate that women with ovarian syndrome is always accompanied by a rise in the concentration of the hormone and also the incidence of obesity and appearance. The hair is in the facial area and around the mouth and chin area with a few menstrual cycles and this is perfectly consistent with [29]. These results may indicate disorders of other hormones in the ovary that affect their concentration on hormones, especially estrogen and progesterone hormones. In addition, women with PCOS have elevated concentrations of the hormone follistatin, which may affect testosterone concentrations. The hormone lipid testicular is one of the factors causing irregular menstrual cycle in women or cancer tumors, especially ovarian cancer and uterus. In addition, the results of women infected with PCOS confirm that they suffer from irregular ovulation. In this case, the menstrual time has a time of about 21 days. The menstrual period increases to about 31 days and causes increase the concentration of hormones in patients which controlling the ovulation process. They had this agreement with a study [30]. If the concentrations of the hormones responsible for ovulation increase, an immature egg is produced and

### References

1. Legro, R.S. and Strauss, J.F. (2002). Molecular progress in infertility: polycystic ovarian syndrome. *Fertil and Steril* . 78: 569-576.
2. Gurnee; Grystal, L, and Illinois. (2009). Infertility with Polycystic ovaries. *Advanced Fertility Center of Chicago, S.C. all right (847) : 662-1818.*
3. Gorry, A.; White, D.M. and Franks, S. (2006). Infertility in polycystic ovary syndrome. *Springer*. 30 (1): 27-33.
4. Flanagan, J.N.; Linder, K.; Mejhert, N.; Dungner, E.; Wahlen, K.; Decaunes, P.; Ryden, M.; Bjorklund, P.; Arver, S.; Bhasin, S. et al. (2009) Role of follistatin in promoting adipogenesis in women. *J Clin Endocrinol Metab* .94:3003–3009.
5. Hansen, J.; Rinnov, A. and Krogh - Madsen R. et al. (2013) Plasma follistatin is elevated in patients with type 2 diabetes: relationship to hyperglycemia, hyperinsulinemia, and systemic low-grade inflammation *Diabetes Metab Res Rev*, 29:463–472 .
6. Hedger, M.P.; Winnall, W.R.; Philips, D.J. and Kretser, D.M. (2011) the regulation & function of activating & follistatin in inflammation and immunity. *Vitam Horm* 85:255-297.
7. Luciano, A. A. (1999) clinical presentation of hyperprolactinemia *J. Repro. Med*, vol.(44): 2 supp) p 1085-1090.
8. Guyton and Hall (2016). *Physiology Review*. 2nd Edition. Elsevier Saunders.
9. Isik, S.; Berker, D.; Tutuncu, Y.A.; Ozuguz, U.; Gokay, F.; Erden, G.; Ozcan, H.N.; Kucukler, F.K.; Aydin, Y. and Guler, S. (2012). Clinical and radiological findings in macroprolactinemia. *Endocrine Apr*; 41(2):327-33.
10. Freeman, M.; Kanyicska, B.; Lerant, A. and Nagy, G. (2000). Prolactin structure, function and regulation of secretion *physiol. Rev.* 80(4) 1523-1631.
11. Basheer, Saad Safloul (2003). *SPSS Arab Institute for Training and Resea.*
12. Suganthi, R.; Manonayaki, S. and Benazir, J.A.F. (2010) Follistatin concentration in women from Kerala with polycystic ovary syndrome *Iranian journal of Reproductive Medicine* Vol.8. No.3 pp: 131-134.
13. El-Shafey, M.; Hegazy, M and El-Zahabi. M. (2016) Clinical significance of Follistatin in obese and none-obese Egyptian polycystic ovary patients *journal of Molecular pathophysiology* Vol(2):10-14.

13. Zongji, S.; Ping, C.X.; Wanxiang, W.; Hong Mei, L. and Xinping, R. (2010). Correlation analysis of B, follistatin and activating A in patients With Ovary syndrome, African Journal of Microbiology Research Vol.4(12) pp.1295-1298.
14. Teede, H.; Ng, S.; Hedger, M. and Moran, L. (2013) Follistatin in polycystic ovary syndrome: relation to metabolic and hormonal markers, metabolic: clinical of experimental 62(10):1394-1400.
15. Gibney, J.; Smith, T.P. and McKenna, T.J. (2005). The impact on clinical practice of routine screening figure a cropt .
16. Biller, B. M. (2001) Diagnostic evaluation of hyper Prolactinemia J. Reprod. Med. 44 (12 suppl) :1093-1099.
17. Prabhaker, V.K. and Davis, J.R. (2008). Hyperprolactinaemia. Best. Pract. Res. Clin. Obst. G.
18. Ferrari, E.; Bossolo, P.A.; Foppa, S.; Dalzano, M.; Comis, S.; Morelli, M.P.; Peveri, V. and Mengozzi, A. (2009). Prolactin secretin in polycystic ovary syndrome . Circadian .
19. Nader, Reem Adib Mohamed (2010). Study of the relationship between hormone lactation and infertility among women in the city of Tikrit and its suburbs. Thesis Masters. Faculty of Science, University of Tikrit
20. Jamiel, Rana Riad (2007). Study of the symptoms of PCOS in women in Iraq. Master Thesis / Basra University / Faculty of Science
21. Lee, S.J. and Mc - Pherron, A.C. (2001) Regulation of myostatin active + tyand muscle growth. Proc Natl Acad Sci USA.98:9306–9311 .
22. Shaw, C.K. sites, K. Patterson, C.S.; Jamison, S. J. Degain, and Laber A.B. (1996) Follicle stimulating hormone increase FSH resptor, J. Endo. Vol (134) p:411-417.
23. Jimenez- Krassel, M. E. Winn, D. Burns, J. L. H. Ireland, and J. J. Ireland (2003) Evidence for a Negative intrafollicular Role for Inhibin in Regulation of Estradiol Production by Granulosa Cells J Endocrinology Vol 144 (5)P: 1876 1886.
24. Melmed, S. and Jameson, L. (2004) In Harrison principles of internal medicin .16th ed New York Mc Graw Hill Professional.
25. Eldar-Geva, T; Groome, N.P; Margalioth, E.J.& Homburg, R.(2001) Follistatin and activi a serum concentrations in obese and non-obese patients with polycystic ovary syndrome. Hum Reprod, Vol 16 (pg 2552-2556) .
26. Veena, H.C.; Manjunatha, S.; Amruta, S. and Hiremath, B. S. (2014) Effect of PCOS on Lipid Profile Scholars Journal of Applied Medical Sciences (SJAMS) (Online) Sch. J. App. Med. Sci., 2(3D): 1153-1155.
27. Yildiz, B.O. and Gedik O. (2004) Assessment of glucose intolerance and insulin sensitivity in polycystic ovary syndrome. Reprod Biomed Online, 8(6): 649-656.
28. Thomas & Rebar, B.O. and Gedik O. (2004) Assessment of glucose intolerance and insulin sensitivity in polycystic ovary syndrome. Reprod Biomed Online, 8(6): 649-656.
29. Basson, R.; Alkaade, S. and Morley, J.E.(2003) The benefit and risks of testosterone replacement therapy, J. Clinical Manag Vol. 5(3) :427-48.
30. Gubayler and Hall (2006) textbook of medical Physiology in: endocrinology and reproduction. 12th ed. Department of physiology and biophysics Jackson mississi PPI.
31. Inoue, S.; Zimmet, P. and Caterson, I.(2009). The Asia- Pacific perspective Redefining obesity and its treatment (Internat). <http://www.diabetes.com.au/pdf/obesity> .
32. King, J.(2006). Polycystic ovary syndrome. J. Midwifery women health; 51(6):415-42.
33. Hasan, A.; Gordon, C.M. (2007). Polycystic ovary syndrome update in adolescence. Cur. Opin. Pediat; 19(4):389-397.

## دراسة الفولستاتين ومستوى الهرمونات الجنسية في النساء مصابات بمتلازمة تكيس المتعدد للمبايض في بغداد

اخلاص عبد الوهاب معروف ، زيد محمد مبارك

قسم علوم الحياة ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق

### الملخص

الهدف من هذه الدراسة هو بحث مستوى الفوليستاتين وعدد من الهرمونات الجنسية في متلازمة تكيس المبايض لدى مجموعة من النساء (70) امرأة مصابة بتكيس المبايض مع عدد من النساء السليمات (20) امرأة كسيطرة. وكان موقع الدراسة في مستشفى كمال السامرائي/ بغداد . وقد تم تشخيص المرضى بجهاز فوق الامواج الصوتية (السونار) من قبل الطبيب المختص. واستمرت مدة الدراسة من شهر ايلول 2016 إلى شهر اذار 2017 أظهرت النتائج وجود ارتفاع عالي المعنوية ( $P<0.01$ ) في تركيز الفوليستاتين لدى النساء المصابات بالمرض مقارنة مع النساء السليمات من ناحية أخرى، كان هناك انخفاض عالي المعنوية ( $P<0.01$ ) في تركيز الهرمون المحفز للجريبات (FSH) في النساء المصابات بمتلازمة تكيس المبايض مقارنة مع السيطرة. أظهرت النتائج وجود ارتفاع عالي المعنوية ( $P<0.01$ ) في تركيز هرمون البرولاكتين و هرمون التستوستيرون في المريضاات اللاتي يعانين من متلازمة تكيس المبايض مقارنة بمجموعة السيطرة.

**الكلمات المفتاحية:** فوليستاتين ، متلازمة تكيس المبايض.