# **Original** Article

# Evaluation of Some Serological Indicators in Women with Polycystic Ovary Syndrome in Baquba , Iraq

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# Abstract:

Polycystic ovary syndrome (PCOS) is receiving increasing attention, due to its association with many health troubles such as infertility and diabetes. The purpose of our study is to estimate the serum level of some indicators in women patients with PCOS. This study was conducted prospectively on 70 participating women who attended Al-Batool Teaching Hospital in Baquba (Iraq), with ages between (18-35) years, from February 2020 to November 2022. All the participating women were separative into two groups: (Control) group included 30 healthy women, and (PCOS) group included 40 women suffer from polycystic ovary syndrome. Ultrasound and analyzes of the sex hormones of the participants were used to confirm the detection of PCOS. Serological biomarkers were measured for both groups, including histidine, ferritin, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and estrogen (E2). Results proven a notable reduction in the serum levels of hepcidin and FSH in PCOS group compared to healthy control group. In contrast, a considerable increases in levels of LH, prolactin, ferritin, and estrogen E2 hormone were observed in patients with PCOS. It was founded that these biochemical indicators may be a reliable diagnostic measure for polycystic ovary syndrome cases.

Keywords: Polycystic ovary syndrome, hepcidin, luteinizing hormone, prolactin.

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# Introduction:

In general, polycystic ovary syndrome (PCOS) can be summarized as a common endocrine disruption in women of childbearing age, and it is a condition characterized by menstrual irregularities with hyperandrogenism. In the last century PCOS was called stein-leventhal syndrome, which is often associated with insulin resistance, hyperlipidemia, and obesity, so it is also considered a metabolic syndrome <sup>[1,2]</sup>. One of the main clinical manifestations is ovarian dysfunction as well as the accumulation of small cysts that usually range (6-10) or more, with a diameter of approximately (4-7) mm surrounded by enlarged inner layers of follicles <sup>[3]</sup>. In addition to polycystic ovaries, infertility and obesity, this disorder is characterized by excessive hairiness, which is called hirsutism <sup>[4]</sup>. In this disorder, the outer layer of the ovary holds together, preventing the mature egg from emerging the ovarian layer, and without the release of this egg, the pregnancy process does not occur <sup>[5]</sup>. In addition, there will be an enlargement in the size of the ovary, which may reach three times its size, as well as an increase in the concentration of ovarian tissue in the middle of the ovary around the cysts. The severeness of this case varies among patients, in some of them the symptoms are almost inconspicuous, and in others are severe and tangible with clearly affect fertility <sup>[6,7]</sup>. Many symptoms are associated with PCOS with varying severity in women, as these

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symptoms are affected by the irregularity of the hormones controlling the menstrual cycle. It should be noted that most of the affected women suffer from infrequent menstruation associated with anovulation and hyperandrogenism<sup>[8]</sup>. Androgen base (testicular fat) is a male hormone that is produced in all women by the ovaries and converted into the main female hormone known as estrogen [9]. In women with PCOS, testosterone production increases more than normal, as does the hormone insulin, which also plays a remarkable role in this. Insulin resistance appears in many patients with this disease, as body tissues resist the effect of insulin and as a result the body is forced to produce more insulin, which in turn affects the ovaries and leads to a hormonal event and increased androgen production, leading to damage to immature follicles <sup>[10]</sup>. On the other hand, abnormal androgen ratio can cause weight gain, acne, excess hair, and irregular ovulation problems <sup>[11]</sup>. In addition, it was found that ovarian syndrome affects the hormone hepcidin, one of the peptide hormones, which is mainly secreted by the liver to regulate iron balance within the body <sup>[12]</sup>. Several studies indicated a relationship between insulin resistance and iron levels in the body, as increased insulin excesses iron storage in the body and raises ferritin levels because the insulin stimulates the intestines to absorb iron. and this indicates an indirect relationship between hepcidin levels and polycystic ovary syndrome <sup>[13]</sup>. Due to the possible interrelation of insulin resistance and iron levels with PCOS, our study was performed to estimate the serelogical levels of some biochemical indicators in women with PCOS in Baguba, Iraq.

# **Patients and Methods:**

In this prospective study, approximately 70 women were enrolled, who admitted to Albatool teaching hospital in Baquba province (Iraq), from February 2020 to November 2022. Of the total of participants in the current study, 40 of them were diagnosed with polycystic ovary syndrome (PCOS), while 30 of them were healthy. All of them underwent а comprehensive clinical examination with ultrasound to find cases of polycystic ovary syndrome by a skilled physician, along with analyzes of sex hormones. All participants were divided into two groups, (Control) for normal ones, and (PCOS) for women suffering from polycystic ovary syndrome ,then a comparison was made of some hormones and

serum indicators between them. The inclusion criteria included women between the ages of (18-30) year old with informed confirmed consent to participate. In contrast, women under the age of 18 who did not consent to participate in the study were excluded. This research was completed after obtaining the acceptance of the ethics council of the local health directorate, and in accordance with the Declaration of Helsinki ethics code for studies involving humans. Blood samples were collected and sera were obtained for all participants from the two study groups. Serum levels of hepcidin, E2, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin hormones were estimated using an immunosorbent assay (ELISA) test method using a measurement kit for each hormone and an ELISA system, according to the commercial manufacturer. The mini VIDAS device was used to measure ferritin concentration, which it works within the technology of enzyme linked fluorescence assay (ELFA). The SPSS system was used to analyze the obtained results, as the arithmetic mean and standard deviation SD were used for the data, in addition to using the T-test to compare the biochemical variables between both groups of the study at the probability standard P less than 5 percent.

#### **Results:**

According to results there was a considerable decrease in serum level of hepcidin of PCOS group  $(818.64\pm104.52 \text{ pg/ml})$ , compared to healthy women  $(1282.84\pm408.42 \text{ pg/ml})$ , as shown in Figure (1).

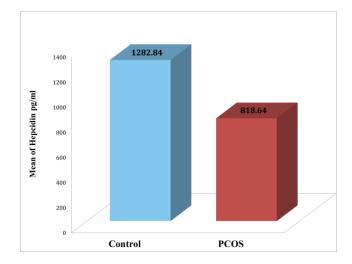


Figure 1: Serum level of hepcidin in both studied groups.

Figure (2) shows the ferritin level, which was (40.99  $\pm$  18.71 ng/ml) in the PCOS patients, while it was in the control women (17.69  $\pm$  8.065 ng / ml). This indicates a clear elevate in serological level of PCOS compared to control subjects.

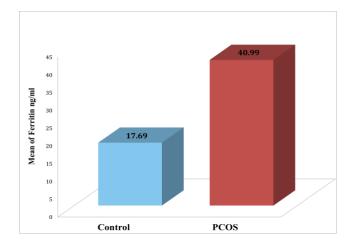
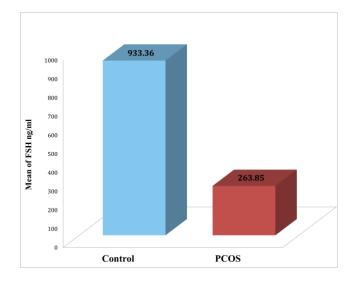


Figure 2: Serum level of ferritin in both studied groups.

As for Figure (3), it shows a lowering in serum level of FSH in PCOS subject ( $263.85 \pm 104.97$  ng/ml) compared to control group ( $933.36 \pm 108.35$  ng/ml).



# Figure 3: Serum level of FSH in both studied groups.

The results also showed that serum level of LH was  $(68.66 \pm 24.06 \text{ ng/ml})$  in women with PCOS, while it was  $(14.68 \pm 9.06 \text{ ng} / \text{ml})$  in the control group. This means a clear increase in the level of LH in patients with PCOS versus to control participitants, as shown in Figure (4).

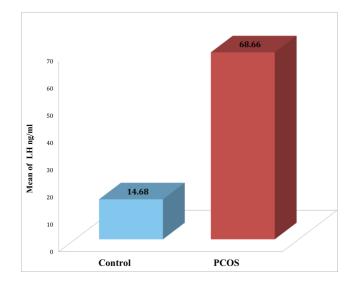


Figure 4: Serum level of LH in both studied groups.

Figure (5) shows an observous raise in the level of the prolactin hormone in patients with PCOS (683.26  $\pm$  236.06 ng / ml) compared to healthy women (208.69  $\pm$  67.06 ng / ml).

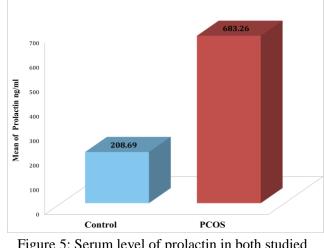


Figure 5: Serum level of prolactin in both studied groups.

Figure (6) shows a notable increase in the estrogen (E2) level in the PCOS group ( $186.66 \pm 48.065$  pg/ml), respected to control women ( $132.66 \pm 8.06$  pg/ml).

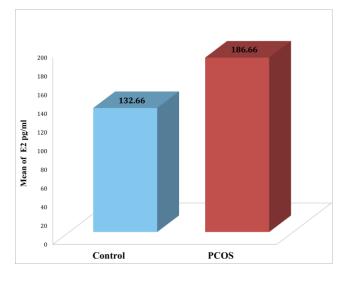


Figure 6: Serum level of estrogen (E2) in both studied groups.

#### **Discussion:**

This study found a clear decline in serelogical level of hepcidin in PCOS patients, and the reason may be due to increased levels of iron. Hepcidin is affected as a result of the accumulation of iron in the body and its increased absorption by the intestines, and this disorder causes an increase in androgen, which is also responsible for disturbing hepcidin level <sup>[14, 15]</sup>. This came in agreement with the results of previous studies carried out by Al-Obeidi and his group, as well as Sam and colleagues<sup>[16,17]</sup>. It should be noted that hepcidin could be a protein involved in the development of metabolic disorders, as it is increased in cases of inflammation and decreased in hyperandrogenism as well as in cases of insulin resistance <sup>[18]</sup>. The results also showed that the value of ferritin level can be adopted as an indicator that helps in diagnosing the case of PCOS development. This is in same line with the results of previous studies by Tiongco et al <sup>[19]</sup> and Ko et al <sup>[20]</sup>, where they confirmed the significant increase in serelogicl level of ferritin in diagnosed polycystic syndrome patients. The main role of ferritin is to sequester iron, and ferroxidase converts Fe II to Fe III, and iron in cellular systems is locked inside the cells and its concentration decreases within the cytoplasm, and it is considered a basic element for the survival of the organism <sup>[21]</sup>. Luteinizing hormone plays an important role in the reproductive process for both females and males. In males, it stimulates the process of spermatogenesis, as it excavates Lan cells located in the environmental cells of the testis

responsible for the secretion of the male hormone, while in females it stimulates ovulation in the ovary after follicle ovulation <sup>[22]</sup>. Measurement of the this hormone level is necessary to detect the ovulation process, as it rises in women in menopause or due to the menstrual cycle caused by primary failure of the ovaries as well as polycystic ovary syndrome. On the other hand, it decreases in cases of estrogen therapy, ovarian or adrenal tumors, or due to pituitary failure <sup>[23]</sup>. In addition, the cause of elevated LH in PCOS patients may be due to hyper sensibility of the pituitary gland to luteinizing hormone inducing gonadotropin-releasing hormone (LHRH), and this causes an excess in the concentricity of GnRH or to abnormality changes in the year of its excretion <sup>[24]</sup>.As for the noticeable increase in the level of the prolactin hormone, it may be due to menstrual disorders that lead to infertility in women through the effect of the prolactin hormone on the FSH hormone and thus its effect on the formation of the egg in the early stages of its appearance, causing a defect in the ovulation process <sup>[25]</sup>. Our results were in agreement with previous similar studies <sup>[24-26]</sup>. The cause of the high serum level of prolactin hormone may be due to the use of medical drugs, and the concentration of this hormone is increased above the normal level in PCOS patients in order to increase the secretion of lactotrophs responsible for the production of the hormone from the anterior lobe of the pituitary gland, which leads to an increase in its secretion, and its increase is associated with the permanent secretion of milk in women, which is observed in some women with PCOS<sup>[27]</sup>. Also, our results in the study are in the same line with other previous studies [28-30], which found a notable augmentation in estrogen E2 hormone level in PCOS compared with control group. Estrogen is very important for ovarian activity, and it is one of the steroid hormones produced by the cells lining the ovaries as a result of the response to FSH. When this hormone is not secreted, it causes the egg not to form, hence not getting pregnant [31,32].

### **Conclusions:**

This study concluded that there was a considerable elevate in both levels of LH, prolactin, estrogen E2, and ferritin in serum of women suffered from polycystic ovary syndrome. Otherwise, there was a clear reduction in the serological levels of hepcidin as well as FSH in women with PCOS. Thus, these biochemical indicators may be reliable diagnostic measurement for cases of polycystic ovary syndrome.

# **References:**

- Parveen S, Khan S, Ahsan H, Manger PT, Gupta B, Alam R. Fat mass and Obesity Associated (FTO) gene and polycystic ovary syndrome: Insight into pathogenesis and association with insulin resistance. Human Nutrition & Metabolism. 2022 Nov 23:200174.
- 2. Witchel SF, Oberfield SE, Peña AS. *Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls.* Journal of the Endocrine Society. 2019;3(8):1545-73.
- 3. Batra R, Dixit R, Gupta S. *Female Infertility*. Diagnostic Radiology: Genitourinary Imaging. 2019 Nov 30:390.
- Kim JH, Kim O, Jung H, Pang Y, Dan H. Body mass index, menstruation, acne, and hirsutism of polycystic ovary syndrome in women: A cross-sectional study. Health Care for Women International. 2022 Mar 4;43(1-3):85-97.
- Ishrat S, Hossain M. Obesity in relation to clinical, endocrine and metabolic parameters in infertile women with polycystic ovary syndrome: the South Asian perspective. Bangladesh J Med Sci. 2021 Jun 18;20(4):864-70.
- Scholes D, LaCroix AZ, Ichikawa LE, Barlow WE, Ott SM. *Injectable hormone contraception and bone density: results from a prospective study*. Epidemiology. 2002 Sep 1:581-7.
- Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls. Journal of the Endocrine Society. 2019 Aug;3(8):1545-73.
- Shan B, Cai JH, Yang SY, Li ZR. *Risk factors of polycystic ovarian syndrome among Li People*. Asian Pacific journal of tropical medicine. 2015 Jul 1;8(7):590-3.
- Ahmad R, Haque M. Obesity inflicted reproductive complications and infertility in men. Bangladesh J Med Sci. 2023 Jan 1;22(1):7-14.
- Barber TM, Franks S. *Obesity and polycystic ovary* syndrome. Clinical endocrinology. 2021 Oct;95(4):531-41.
- Tirgar-Tabari S, Sharbatdaran M, Manafi-Afkham S, Montazeri M. Hyperprolactinemia and hirsutism in patients without polycystic ovary syndrome. International journal of trichology. 2016 Jul;8(3):130.
- 12. Nemeth E, Tuttle MS, Powelson J, Vaughn MB, Donovan A, Ward DM, Ganz T, Kaplan J. *Hepcidin regulates cellular iron efflux by binding to ferroportin*

and inducing its internalization. science. 2004 Dec 17;306(5704):2090-3.

- Gulec S, Anderson GJ, Collins JF. *Mechanistic and* regulatory aspects of intestinal iron absorption. American Journal of Physiology-Gastrointestinal and Liver Physiology. 2014 Aug 15;307(4):G397-409.
- Luque-Ramírez M, Álvarez-Blasco F, Alpañés M, Escobar-Morreale HF. *Role ofdecreased circulating hepcidin concentrations in the iron excess of women with the polycystic ovary syndrome*. J Clin Endocrinol Metab. 2011;96:846–52.
- 15. Datz C, Felder TK, Niederseer D, Aigner E. Iron homeostasis in the metabolic syndrome. Eur J Clin Invest. 2013;43:215–24.
- Al-Obaidi WM, Al-Izzi MH. Study of Hepcidin and Many Physiological and Hematological Parameters in Women with Polycystic Ovary in Kirkuk City. Annals of the Romanian Society for Cell Biology. 2021 Apr 1:7494-504.
- 17. Sam AH, Busbridge M, Amin A, Webber L, White D, Franks S, et al. *Hepcidin levels in diabetes mellitus and polycystic ovary syndrome*. Diabet Med. 2013;30:1495–9.
- Ahmed HH, Fadl NN, Kotob SE. Impact of Long Term Metformin Therapy on Hepcidin and Iron Status in Type II Diabetic Patients. International Journal of Pharmaceutical and Clinical Research. 2015;7:185– 93.
- Tiongco RE, Rivera N, Clemente B, Dizon D, Salita C, Pineda-Cortel MR. Serum ferritin as a candidate diagnostic biomarker of polycystic ovarian syndrome: a meta-analysis. Biomarkers. 2019 Jul 4;24(5):484-91.
- Ko PC, Huang SY, Hsieh CH, Hsu MI, Hsu CS. Serum ferritin levels and polycystic ovary syndrome in obese and nonobese women. Taiwanese Journal of Obstetrics and Gynecology. 2015 Aug 1;54(4):403-7.
- St John AT, Stuart KA, Crawford DH. Testing for HFE-related haemochromatosis. Australian Prescriber. 2011 Jun 1;34(3):73-6.
- 22. Broer SL, van Disseldorp J, Broeze KA, Dolleman M, Opmeer BC, Bossuyt P, Eijkemans MJ, Mol BW, Broekmans FJ, IMPORT Study Group, Broer SL. Added value of ovarian reserve testing on patient characteristics in the prediction of ovarian response and ongoing pregnancy: an individual patient data approach. Human reproduction update. 2013 Jan 1;19(1):26-36.
- 23. Boulpaep EL, Boron WF, Caplan MJ, Cantley L, Igarashi P, Aronson PS, Moczydlowski E. *Medical physiology: a cellular and molecular approach.* 2009: 27.
- 24. Mubarak ZM, wahab Maarouf IA. Study of follistatin and sex hormones level in women with polycystic

*ovarian sayndrome in Baghdad*. Tikrit Journal of Pure Science. 2018 Jun 3;23(4):1-6.

- 25. Hart R, Hickey M, Franks S. Definitions, *prevalence* and symptoms of polycystic ovaries and polycystic ovary syndrome. Best Practice & Research Clinical Obstetrics & Gynaecology. 2004 Oct 1;18(5):671-83.
- 26. Shah AK, Sarin M, Karunanand B, Mohapatra S, Bhat SA. Association of hormonal status with anthropometric & biochemical parameters in women with polycystic ovarian syndrome. hypertension. 2017;3(4):5.
- King J. Contraception and lactation. Journal of midwifery & women's health. 2007 Nov 1;52(6):614-20.
- Chen J, Shen S, Tan Y, Xia D, Xia Y, Cao Y, Wang W, Wu X, Wang H, Yi L, Gao Q. *The correlation of aromatase activity and obesity in women with or without polycystic ovary syndrome*. Journal of Ovarian Research. 2015 Dec;8(1):1-6.
- 29. Khalil RA. *Estrogen, vascular estrogen receptor and hormone therapy in postmenopausal vascular disease.* Biochemical pharmacology. 2013 Dec 15;86(12):1627-42.
- Al-Juaifari BJ, Al-Jumaili EF. Correlation of Body Mass Index and Some Hormones (Estradiol, Luteinizing, Follicle Stimulating Hormones) with Polycystic Ovary Syndrome among Young Females [20 to 35 Years]. Biomedical and Pharmacology Journal. 2020 Mar 28;13(1):193-8.
- Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocrine reviews. 2016 Oct 1;37(5):467-520.
- 32. Kuiri-Hänninen T, Haanpää M, Turpeinen U, Hämäläinen E, Seuri R, Tyrväinen E, Sankilampi U, Dunkel L. Postnatal ovarian activation has effects in estrogen target tissues in infant girls. The Journal of Clinical Endocrinology & Metabolism. 2013 Dec 1;98(12):4709-16.