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Research Article

# The role of Myeloperoxidase, reproductive hormones and thyrodism in polycystic ovary syndrome patients

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Abstract :

This study was conducted at the Infertility Center at Al-Batool Teaching Hospital for Women and Children in Dyala Governorate from 08/22/2020 to 12/1/2020. It was followed up of 100 cases of women suffering from polycystic ovaries, and it was compared to the control group, which included 50 standard points and then confirmed. They are free of chronic diseases such as thyroid disease and diabetes .

The study aims to assess the clinical and hormonal status by measuring LH, FSH, melatonin, , and the aetiology and risk factors for infertile women with polycystic ovary syndrome. . The concentration of hormones was measured for both women with the syndrome and those without the syndrome, including LH, as it was observed that the level of LH concentration increased significantly in women with the syndrome, as it reached a concentration of (17.61 +_4.320) compared to the non-affected (4.53 +_1.86). The level of FSH hormone reached its concentration in women Female patients with the syndrome, as its attention reached (3.20 +_1.57) compared with the control group (7.53 +_1.68) and The concentration of the myeloperoxidase enzyme was measured. Its attention was (2.65 +_1.22) compared with the control group (1.12 +_0.53).

Key word : Poly cystic Ovary Syndrome, LH,FSH, Myeloperoxidase

## 1-Introducation:

### 1-Poly Systic Ovary Syndrome :-

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age (1), it is a condition ssociated with chronic anovulation, insulin resistance, and androgen excess(2). Affected individuals typically present to clinical attention during evaluation for infrequent menses, infertility, and/or hirsutism(3). The prevalence of PCOS among women of reproductive age in the general population has been estimated at 4% to 12%(4), the prevalence and characteristics of women with PCOS among broader, ethnically diverse populations and within usual care settings are less well understood, it appear to be higher (from 37% to 90%) in women with menstrual abnormalities and also is increased in the presence of certain diseases(5)

In addition to reproductive and hyper androgenic concerns, PCOS is also associated with a number of metabolic perturbations that ultimately may contribute to an excess risk for cardiovascular events. Women with PCOS are more likely to be insulin resistant, overweight, and obese, and several studies have demonstrated that PCOS is associated with an increased risk of glucose intolerance and type 2 diabetes mellitus, independent of body mass index (BMI)(6). Finally, a growing body of evidence suggests an association between PCOS and hypertension and markers of subclinical atherosclerosis and vascular dysfunction (5)

Excess insulin appears to increase production of androgen. Levels of androgen that are higher than normal can lead to acne, excessive hair growth, weight gain, and problems with ovulation(5). The cutaneous manifestations of increased androgenic hormones are hirsutism, acne, seborrhea, alopecia, obesity, and acanthuses nigricans(2).

On the basis of the National Institutes of Health (NIH) meeting in 2003, any two of the three are sufficient to confirm the diagnosis of PCOS, specific morphology of polycystic ovaries in ultrasonography findings, hyperandrogenism (biochemical or clinical), and oligo- or amenorrhea. (7)

**2- Biomarkers of Polycystic ovary syndrome:**

**Follicle stimulating hormone (FSH)**

Follicle-stimulating hormone is a glycoprotein (polypeptide hormone) that is manufactured and excreted by the basophilic cells gonadotropins of the \anterior lob of the pituitary gland. FSH adjusts the human body's development, growth, pubertal maturation and reproductive processes. In reproduction process, FSH and LH hormones are performed synergistically (8). FSH has β subunit consist of amino acid, which provides its particular biologic action and is responsible for FSH receptors interaction (9). In female, FSH starts follicle growth which directly influences granulosa cells with the accompanying raise of inhibin-B, then decreases FSH rates in late follicular phase. This looks essential in choosing only the most mature follicle for advance in ovulation. When the luteal phase ends, there is a small increase in levels of FSH which appears to be essential in initiating the subsequent ovulatory cycle. In the pituitary gland, the excretion of FSH is managed by the pulses of GnRH) and the pulses, in turn, are subjected to the feedback of estrogen from the gonads (10).

**Luteinizing Hormone (LH)**

Luteinizing hormone is renowned as lutropin, created and excreted in the anteriorly pituitary gland by gonadotropin (11). In women, an extreme increase in LH causes ovulation, and growth of corpus luteum (12). LH is a protein dimer that contains two glyco-peptides subunits which are termed as (α and β) subunits, and are non-covalently associated. α subunit of LH is identical, and contains (13) amino acids in human, while β subunits vary, and contain (14) amino acids which confer its specific biological activity which is responsible for the specificity of LH receptor interactions. The biologic half-life of the LH is twenty minutes, shorter than FSH that is (3-4 hours). At menstrual period, FSH initially begins follicular development (15). figure (1-8). As estrogens increase, LH receptors are activated on maturing follicles which contain an increasing level of estradiol. Finally at follicle maturation, the increase in estrogen contributes to the (positive feedback) impact through the hypothalamic interface, a releasing of LH over a period of (24-48) hour. Increasing LH leads to ovulation through not releasing the egg only, but also to start the change of the remaining follicle into a corpus luteum, which in effect generates progesterone to prepare the endometrium for probable implantation. Luteinizing hormone is required to maintain function of luteal during the first 2 weeks,

and promotes ovarian theca cells that provide androgens and hormonal precursors for estradiol production (16).

**Myeloperoxidase :-**

MPO is a myeloid-lineage restricted enzyme with strong antibacterial properties. During myeloid cell differentiation, MPO is largely expressed by neutrophils [17] where is located within azurophilic granules [18]. In addition, studies have also shown that MPO is produced by monocytes/macrophages including peritoneal macrophages and central nervous system (CNS) microglial cells, at least during pathological conditions [19]. In bacterial infection, neutrophil-derived MPO generates the potent bactericidal compound hypochlorous acid (HClO) [20]. Since neutrophils are important contributors to autoimmune disease pathogenesis it is not surprising that MPO is generally regarded as pathogenic during autoimmune disease progression, although some studies have reported contrary results [21]. The importance of neutrophils in the pathogenesis of a number of autoimmune diseases and the lack of safe and effective strategies to specifically target them, makes MPO a potential therapeutic target. Over the past decade, the finding of large quantities of myeloperoxidases in atheromatous plaques has led torecognition of their important role in the atherosclerotic process [22].

**2-Material and Methods**

**1- Chemicals:-**

All chemicals and reagents that were used in this study are illustrated in Table (1).

**Table (1): List of chemicals and reagents used.**

| No | Chemicals | Company |
|---|---|---|
| 1 | LH (luteinizing hormone) Kit | Roche-USA |
| 2 | FSH (follicle stimulating hormone) Kit | Roche-USA |
| 3 | Myeloperoxidase ELISA Kit | Bioassay |

**2- Instruments:-**

All our instruments that used showed in Table (2-2).

Table (2-2): List of Laboratory Equipment .

| No | Instruments | Company |
|---|---|---|
| 1 | Cooling centrifuge | Eppendrof-Germany |
| 2 | Centrifuge | KOKUSAN-Japan |
| 3 | Deep Freezer | Karl Kolb- Germany |
| 4 | ELISA Microplate Reader &Washer | Bio Tek-USA |
| 5 | ELISA system | Bio test-Germany |
| 6 | Water bath | Memmert-Germany |
| 7 | Cobas 411 system | Roche-USA |

**3-Samples Collection and Preparation:**
**Patients and Control Groups:**

One hundred of Polycystic ovary syndrome (PCOS) patients, throughout the study for the period from December 2019 to March 2020 in Baquba teaching Hospital, The medical history was taken, body weight , height were measured as well as body mass index (BMI). The age of these patients ranged from (18 to 40) years. All patients were subjected to a personal interview using a specially designed questionnaire format full history with detailed information (Appendix I). The diagnoses of the disease were confirmed by biochemical examination and ultrasound. Which was carried in the laboratories of the hospital mentioned above for comparison, fifty healthy were included in the study as control with matched body weight, height and their body mass index (BMI).

**Blood Samples Collecting:**

Ten milliliter of blood were collected in to test tubes without anticoagulants. After coagulation, the samples were centrifuged for ten min and the serum stored on an ice bath and was used in the same day for the enzymatic activity assays, Liver function test and mineral determination. The remainder of the sera were stored at -20°C, to be used for other parameters estimation. The sera samples should be unhemolyzed and non-jaundice to avoid any interference in the obtained results**.**

**- Determination of Some Biochemical Parameters in Serum:**
**- Hormones:**
**- Luteinizing hormone(LH) and follicle stimulating hormone (FSH):-**
**-** Sandwich principle. Total duration of assay: 18 minutes

**- Myeloperoxidase Hormone**
- This kit is an Enzyme-Linked Immunosorbent Assay (ELISA).

**3-Results:**

**1- Description of the Study Groups:**

The total number of (150) individual samples were included in the present study, the control group consists of (50) healthy individual samples, while the PCOS patients were (100) individual samples.

**2-Hormonal profile**

Table (3) shows comparison of the mean value of selected hormonal profile between PCOS patients and controls group containing (FSH, LH , Myeloperoxidase).

**Table (3) Comparison between PCOS patients and controls groups according to the selected Hormonal profile**

| Groups | | N | Mean | SD | P value |
|---|---|---|---|---|---|
| LH | Patients | 100 | 17.61 | 4.32 | 0.002** |
| | Controls | 50 | 4.53 | 1.86 | |
| FSH | Patients | 100 | 3.20 | 1.57 | 0.001*** |
| | Controls | 50 | 7.53 | 1.68 | |
| Melatonin | Patients | 100 | 64.85 | 24.43 | 0.001** |
| | Controls | 50 | 19.28 | 9.20 | |

**-Luteinizing Hormone (LH)**

Result of current study shows the mean value was high for LH hormones patients (17.61±4.32) than control (4.53±1.86) with high significant different (P<0.05) between study groups as shown in figure (3).

The finding result is in line with Hashemi *et.al* in 2016(26), Moustafa *et al* in 2019 (27) and Abdulwahid *et al* in 2019 (28) since they found that mean values of serum-LH for patients were significantly higher than those of controls.

In PCOS, a unique trait is the unsuitable GnRH excretion with high levels of LH and relatively low levels of FSH(29). By their aromatization to the estrogens, the androgens are able to alter (gonadotropin release), and there are some theories which tried to clarify the causes of elevate LH in PCOS, as primary irregularity of hypothalamic organization of LH as an elevate LH pulse frequency (30).

**- Follicle Stimulating Hormone (FSH)**

Result of current study shows the mean value was high for FSH hormones patients (3.20±1.57) than control (7.43±1.68) with high significant different (P<0.05) between study groups as shown in figure (3.1).

The finding result is in line with AL-Deresawi *et.al* in 2015 (245), Shoaib *et al* in 2015 (31) and Oyebanji *et al* in 2018 (32) since they have observed that the mean values of patients serum-FSH was significantly lower than those of controls.

In usual menstruation, the elevation of plasma-FSH through the (luteal-follicular change) is crucial for develop follicle and consequently ovulation. In hyperandrogenemic female who destined to improve PCOS, different from natural early pupery, decrease levels of FSH is probably due to the fact that the nocturnal elevate in the ovarian steroid hormones may be not sufficient to repress the GnRH pulse generator, that leads to a continuous increases rapid pulse frequency of LH, and decrease FSH manufacture which causes insufficient follicular growth(33),

**-Myeloperoxidase:-**

Result of current study shows the mean value was high for Myeloperoxidase patients (2.56±1.22) than control (1.12±0.53) with high significant different (P<0.05) between study groups as shown in figure (3.1).

The finding result is in line with (34) since they concluded that mean values of patients serum-MPO were significantly higher than those of controls.

To the best of our knowledge, this is also the first study investigating serum MPO and ADA activities in women with PCOS. In the present study, serum MPO level was higher in the PCOS group compared with the controls. Sasıkala et al. [35] indicated that MPO was an excellent inflammatory marker and showed elevated MPO levels in the ovarian and uterine tissues of PCOSinduced rats. Dursun et al. [36] also found higher MPO levels in gingival cervicular fluid of women with PCOS. One of the mechanisms underlying the pathogenesis of PCOS is chronic low-grade inflammation and MPO is an enzyme released from activated neutrophils, and macrophages. Therefore, the finding of increased monocyte and neutrophil counts observed in our study is compatible with the elevated serum MPO activity in the women with PCOS. Besides showing inflammation, [37,38)

**3-Phenotypic Patterns & Pathogenic of PCOS:**

The resultss of mean anthropometric are indices in sera of all studied groups. Result of current study shows the percentage of patients have BMI>25 show (83.0%) was more than BMI<25 or 25 with high significant different (P<0.001), while the percentage for patients have Acne 88.0% was more than no have Acne (12.0%) with high significant different (P<0.001)

**Table (2) Comparative current study parameters between study groups.**

| | | Count | Percent | P value |
|---|---|---|---|---|
| BMI | <25 | 7 | 7.0% | 0.001*** |
| | 25 | 10 | 10.0% | |
| | >25 | 83 | 83.0% | |
| Acne | Yes | 88 | 88.0% | 0.001*** |
| | No | 12 | 12.0% | |
| hair show | Yes | 94 | 94.0% | 0.001*** |
| | No | 6 | 6.0% | |
| DM | Yes | 56 | 56.00% | 0.23 |
| | No | 44 | 44.00% | |
| infertility | Firstly | 76 | 76.00% | 0.001*** |
| | Secondly | 24 | 24.00% | |
| Genetics | Yes | 78 | 78.0% | 0.001*** |
| | No | 22 | 22.0% | |
| menstruation | Yes | 96 | 96.0% | 0.001*** |
| | No | 4 | 4.0% | |

One of the clinical features of PCOS is obesity with menopause or irregular menstruation and abnormal hair growth in some parts of the body (hirsutism) and infertility. However, not all females with polycystic ovary disease are obese and not all obese females have polycystic ovary syndrome (39).

the percentage for patients have hair show was 94.0% more than no have hair show (6.0%) with high significant different (P<0.001) Hirsutism can be defined as excessive (unwanted) hair outgrowth in some areas usually associated with male sexual characteristics, i.e. in the chest area, chin area of the face, lower abdomen, buttocks and up thighs. Hirsutism appears due to the effects of androgen on the grease unit and is usually associated with oily skin and acne. This is often due to the increased production of androgen from the ovaries , Androgen overproduction in females with PCOS causes a series of skin changes such as acne, hirsutism and androgenic alopecia, One of the factors that contribute to appear some symptoms of PCOS such as hirsutism, acne, and infertility, the high concentrations of testosterone(40)The results noticed by this study were in agreement with Azziz et. al (41) and Ovalle and Azziz (42).

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