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Clinical and Biochemical Study of the Impact of Anti Insulin-Antibody and Insulin-Like Growth Factor on Polycystic Ovary Syndrome (PCOS)

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Abstract

The study focused on the Anti-Insulin Antibody and Insulin-Like Growth Factor and its relationship with the Polycystic Ovary Syndrome (PCOS) in women. Was collected 61 samples of PCOS women and 45 samples as a control group. The results showed a significant increase in the Insulin-Like Growth Factor-1 (IGF-1), insulin, insulin resistance, follicle-stimulating hormone, ovulation hormone, estrogen hormone and progesterone hormone with (P = 0.05, P = 0.007, P = 0.001, P = 0.001, P = 0.006, P = 0.001, and P = 0.001) respectively, in women with PCOS. Some PCOS women who are overweight have a high body mass index. Obesity is the leading cause of period and fertilization problems. Finally, the study showed that there is a strong relationship between Anti-Insulin Antibody's Influence and Insulin-Like Growth Factor on PCOS..

Keywords: PCOS, Anti Insulin Antibody (AIA), Insulin-Like Growth Factor-1 (IGF-1), Insulin (INS), HOMA-IR, Sex hormones

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دراسة سريرية وبيوكيميائية لتأثير الأجسام المضادة للأنسولين وعامل النمو المشابه للأنسولين على متلازمة تكيس المبايض (PCOS)

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المستخلص

ركزت الدراسة على الأجسام المضادة للأنسولين وعامل النمو الشبيه بالأنسولين وعلاقتها بمتلازمة المبيض المتعدد الكيسات (PCOS) لدى النساء. تم جمع 61 عينة من نساء متلازمة تكيس المبايض و 45 عينة كمجموعة ضابطة. أظهرت النتائج زيادة معنوية في كل من عامل النمو الشبيه بالأنسولين-1 (IGF-1)، الأنسولين، مقاومة الأنسولين، الهورمون المنبه للجريب، هورمون التبويض، هورمون الاستروجين وهورمون البروجسترون عند مستوى احتمالية (P = 0.05، P = 0.007، P = 0.001، P = 0.001، P = 0.006، P = 0.001 و P = 0.001) على التوالي، في النساء المصابات بمتلازمة تكيس المبايض. كما ان بعض النساء المصابات بمتلازمة تكيس المبايض ذوات الوزن الزائد لديهن مؤشر كتلة جسم مرتفع. السمنة هي السبب الرئيسي لمشاكل الدورة الشهرية والإخصاب. وأخيراً أظهرت الدراسة أن هناك علاقة قوية بين تأثير الأجسام المضادة للأنسولين وعامل النمو الشبيه بالأنسولين على متلازمة تكيس المبايض.

الكلمات المفتاحية : متلازمة تكيس المبايض، الأجسام المضادة للأنسولين (AIA)، عامل النمو الشبيه بالأنسولين -1 (IGF-1)، الأنسولين (INS)، مقاومة الانسولين ، الهرمونات الجنسية.

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Introduction

PCOS, which includes gonad dysfunction and metabolic abnormalities, is the most common endocrine condition in females of reproductive age. According to recent prevalence estimates, full hyperandrogenism and ovulation affect 5-10% of premenopausal women [1]. According to the data, PCOS women are more likely to acquire non-insulin-dependent diabetes due to particular anomalies in insulin function. Several causes have

been linked to the syndrome's emergence, which may eventually lead to female infertility owing to follicular failure to mature and deposit the fertilized egg [2,3].

While PCOS impacts the whole menstrual cycle, as it begins to collapse in the follicular phase, the anterior pituitary gland produces a significant quantity of LH, at least twice as much as excessive ovulation hormone stimulates theca cells to leak excessive quantities of Androstenedione, which is more harmful. Excess androstenedione is released into the bloodstream by those granulosa cells, as well as some adipose tissue converts it to estrone (Estrone, like estradiol, belongs to the estrogen family and acts as a negative feedback signal, preventing FSH secretion by the anterior pituitary gland) [4].

Hirsutism, or hair development on the chin, upper lip, chest, and back, is a side effect of PCOS, due to high levels of androstenedione. It can also cause male pattern baldness, which is characterized by hair thinning beginning at the top of the head and acne on the chest, back, and face [5]. An amenorrhea is the absence of ovulation. (no menstruation) or oligomenorrhea (irregular periods), both of which can lead to infertility [6]. Insulin resistance increases the risk of being overweight or obese, as well as the development of acanthosis nigricans (dark, velvety patches in the neck, thigh, and underarm wrinkles) [7, 8].

Insulin-like growth factors are classified into two types: IGF-1 and IGF-2. Despite their identical names, these two factors differ in terms of particular activities on tissues because they bind to and activate distinct receptors, and the principal function of IGFs is cell proliferation [9]. Most of the effects of pituitary growth hormone (GH) are acted upon by IGFs, primarily IGF-1 [10].

Methods and Materials Data collection

This study is conducted in several hospitals in AL-Salaam/ Al-Mosul, Iraq, obtained from December 29, 2021, to April. 20, 2022,

Sixty-one PCOS women patients participated in this study. Their ages varied from 20 to 43, and their BMI ranged from 18.59 to 41.40 kg/m^2. Forty five women aged 20 to 42 years participated in this study as a control group. BMI ranged between 19.05 and 31.24 kg/m^2.

For all samples during the early follicular phase, blood samples were obtained in the morning following 12 hours of fasting (day two or three of the menstrual cycle) for sex hormones (LH, FSH, E2) and INS, IGF-1, AntiInsulinAb (AIA). While progesterone is at ovulation (day 13 or 14 of the menstrual cycle) for both groups [11]. PRG, E2, LH, and FSH variables were measured using a specific kit (Bio Merieux Kits) from Minividas-France. Cobas-e411 uses Roche kits for the INS and IGF-1 variants and Alergia uses a special kit (Orgentec Kits) for AIA. While Body Mass Index (BMI) was calculated using the equation (1):

$$\mathbf{BMI_{(Kg/m2)} = weight_{(Kg)} / length_{(m2)}} \quad (1)$$

Finally, SPSS software was used to analyze the data. Where * indicates significant differences at P≤0.05, ** indicates significant differences at P0.001, and finally NS means no significant differences

Statistical Analysis:

Analysis of the data was conducted using SPSS tools. T-test, Duncan test was used to compare the parameters between the total number of control and patients, based on the occupancy at p≤0.05, p≤0.01, and p≤0.001, respectively, and Pearson correlation coefficient test. The Duncan-tests is

used to indicate the differences when comparing more than two groups of the same chemical parameter (a, b, ab means the difference, and if all are the same, it indicates no significant statistical difference), which is identical to the p-value.

Ethical Approval:

The study was conducted under all applicable national legislation, institutional policy, and the Helsinki Declaration ideals, and was approved by the author's institutional review board No. 46692 at December 29, 2021.

Results and Discussion

Comparison of hormonal and biochemical concentrations variables between women with PCOS and healthy women:

The results of this study, as shown in Table-1, when comparing the hormonal and biochemical concentration variables between females with PCOS and healthy women, showed a highly significant in the level of Insulin Antibody (AIA), Insulin-Like Growth Factor-1 (IGF-1), insulin, insulin resistance, follicle-stimulating hormone, ovulation hormone, estrogen hormone and progesterone hormone at P = 0.03, P = 0.05, P = 0.007, P = 0.001, P = 0.001 P = 0.006, P = 0.001, and P = 0.001) respectively.

Table (1): Comparison of hormonal and biochemical concentrations variables between women with PCOS and healthy women

Hormonal & Biochemical Variables	Control Group (No. 45) Mean ± SD	PCOS Group (No. 60) Mean ± SD	P_{Value}
Insulin Antibody (AIA) U/ml	2.79 ± 2.03	3.69 ± 3.2	0.03*
Insulin-Like Growth Factor-1 (IGF-1) ng/ml	171.8 ± 44.05	187.5 ± 60.05	0.05*
Insulin (INS) µU/ml	11.80 ± 3.1	14.78 ± 6.7	0.007**
HOMA-IR	2.17 ± 0.5	3.09 ± 1.4	0.001**
Follicle-Stimulating Hormone (FSH) mlU/ml	5.21 ± 1.7	7.04 ± 3.1	0.001**
Ovulation Hormone (LH) mlU/ml	5.98 ± 1.8	8.29 ± 5.2	0.006**
LH/FSH	1.23 ± 0.4	1.34 ± 0.8	NS
Estrogen (E2) pg/ml	64.9 ± 31.5	88.88 ± 28.6	0.001**
Progesterone (P4) ng/ml	2.29 ± 0.2	0.20 ± 0.1	0.001**

* Significant differences at P≤0.05, **Significant differences at P≤0.001, NS=No significant differences

The concentration of hormonal and biochemical variables in women with PCOS compared to their BMI:

The results in this study, as shown in Table-2, revealed a significant rise in the level of insulin and insulin resistance at (P = 0.001 and P = 0.001) respectively.

Table (2): The concentration of hormonal and biochemical variables in women with PCOS compared to their BMI

BMI / Hormonal & Biochemical Variables	18-24.9 No. 20 Mean ± SD	25--29.9 No. 22 Mean ± SD	30-34.9 No. 15 Mean ± SD	35-39.9 No. 4 Mean ± SD	P_{Value}
Insulin Antibody (AIA) U/ml	1.61±0.5 a	3.76±3.1 b	6.0±5.85 ab	6.4±0.1a	0.05*
Insulin-Like Growth Factor-1 (IGF-1) ng/ml	217.3±69 a	179.3±43 ab	171.8±61.9 ab	142.5±7.4 b	0.03*
Insulin (INS) µU/ml	9.56±5.2 c	16.05±4.1 b	16.63±6.4 b	27.0±0.3 a	0.001**
HOMA-IR	1.92±1.03 c	3.25±0.7 b	3.53±1.4 b	6.31±0.4 a	0.001**
Follicle-Stimulating Hormone (FSH) mlU/ml	5.26±1.4 b	8.47±3.3 a	8.06±3.5 a	4.20±0.08 b	0.001**
Ovulation Hormone (LH) mlU/ml	11.40±6.9 a	7.49±4.1 ab	6.42±2.4 b	4.22±0.8 b	0.006**
LH/FSH	2.10±0.9 a	0.97±0.5 b	0.97±0.6 b	1.007±0.2 b	0.001**
Estrogen (E2) pg/ml	63.90±56.3a	116.1±12.2 a	76.74±55 a	109.6±84.6 a	NS
Progesterone (P4) ng/ml	0.22±0.2 a	0.23±0.2 a	0.105±0.1 a	0.18±0.1a	NS

* Significant differences at P≤0.05, ** Significant differences at P≤0.01, NS=No significant differences

Correlation of the effect of INS for PCOS women, depending on hormonal and biochemical variables:

The results listed in Table-3 prove that there is a correlation factor for PCOS patients with the level of Insulin (INS).

Table (3): Correlation of the effect of INS for PCOS women, depending on hormonal and biochemical variables

Hormonal & Biochemical Variables	r correlation value	P_{Value}
Insulin Antibody (AIA) U/ml	-0.177	NS
Insulin-Like Growth Factor-1 (IGF-1) ng/ml	-0.271	0.03*
Follicle-Stimulating Hormone (FSH) mlU/ml	0.152	NS
Ovulation Hormone (LH) mlU/ml	-0.104	NS
Estrogen (E2) pg/ml	0.336	0.008**
Progesterone (P4) ng/ml	0.082	NS
BMI Kg/m^2	0.626	0.001**

*Significant differences at P≤0.05, **Significant differences at P≤0.01, NS=No significant differences

Correlation of the effect of (IGF-1) for PCOS women, depending on hormonal and biochemical variables:

The findings in Table-4 show that there is a correlation factor for PCOS patients with the level of IGF-1.

Table (4): Correlation of the effect of Insulin-Like Growth Factor-1 (IGF-1) for PCOS women, depending on hormonal and biochemical variables

Hormonal & Biochemical Variables	r correlation value	P_{Value}
Insulin Antibody (AIA) U/ml	-0.316	0.001*
Insulin (INS) µU/ml	-0.271	0.034**
Follicle-Stimulating Hormone (FSH) mlU/ml	-0.123	NS
Ovulation Hormone (LH) mlU/ml	0.355	0.005**
Estrogen (E2) pg/ml	0.285	0.026*
Progesterone (P4) ng/ml	0.133	NS
BMI Kg/m^2	-0.351	0.006**

*Significant differences at P≤0.05, ** Significant differences at P≤0.01, NS=No significant differences

The results in Table-1 showed the women with PCOS. Insulin resistance leads to an increase in the availability of free androgen, and thus a change in follicular development and granulosa cell function [12]. An increase in insulin concentration in women with PCOS reduces the level of Sex Hormone Binding Globulin (SHBG), which enhances the bioavailability of the level of insulin. Also, free testosterone: These women have abnormal gonadotropin concentrations and androgen synthesis from the adrenal glands and ovaries that are stimulated by a high level of insulin [13].

One of the neuroendocrine characteristics that are believed to be in PCOS is the rapid pulsation of gonadotropin-releasing hormone (GnRH), which causes the pituitary gland to prefer the formation of ovulation hormone over follicle-stimulating hormone and contributes to an increase in LH concentrations and thus changes LH levels. Inadequate FSH levels contribute to poor follicle growth, while increased levels of LH promote androgen production from the ovary [14]. The reason for the high level of insulin antibodies may be due to the fact that the immune system of women with the syndrome is affected by the increase in estrogen hormone and becomes more susceptible to an autoimmune reaction, because estrogen stimulates antibodies, which makes the immune system send signals that lead to autoimmunity [15]. The cause of high estrogen hormone in women with the syndrome can be attributed to the high percentage of fat in the body, which in turn can raise the percentage of estrogen in the body [16].

While it showed a significant decrease in the level of the hormone progesterone at (p=0.001) in women with PCOS, the decrease in the hormone progesterone in women with PCOS may be obesity that has negative effects on the fertility of women

through insulin resistance, hyperandrogenism and injury Chronic Anovulation [17,18].

Table-2 shown that when there is a lot of excess insulin in the bloodstream, it signals the body to put this extra sugar into storage in the liver and muscles, yet the body begins to store the extra sugar as fat and this of course causes weight gain [19]. Obesity is associated with an increased risk of insulin resistance with PCOS in women and diabetes (type 2). Adipose tissue in people with obesity produces more non-esterified fatty acids, glycerol, and pro-inflammatory cytokines. Pro-inflammatory cytokines and many other variables have a role in the development of insulin resistance [20]. The results also showed a significant decrease in the level of follicle-stimulating hormone, ovulation hormone, LH:FSH ratio, and insulin-like growth factor-1 at ($p = 0.001$), ($p = 0.006$), ($p = 0.0001$), ($p = 0.030$) on the Straight for women with PCOS with a body mass index. High BMI in some women with PCOS who are overweight and obese is the main known cause of irregular periods and ovulation [21]. A low level of IGF-1 in the serum of overweight PCOS patients may indicate a decrease in its production, and in particular, obese patients show reduced secretion of growth hormone (GH) [22].

The results in Table-3 confirm that the increase in Insulin concentration is a sign that increases the risk factors for PCOS. Where the results showed that there is a significant positive correlation between PCOS and the level of Insulin (INS) in each of the follicle-stimulating hormone (FSH) estrogen hormone, progesterone hormone, and BMI, as their concentration increases with the increase in the level of Insulin (INS) and vice versa The positive correlation between insulin and estrogen can be explained by the fact that estrogen has a key role in regulating the reproductive system in addition to improving insulin activity, so high levels of insulin lead to disruption of the work of estrogen hormone and the emergence of symptoms of high levels such as heavy bleeding during menstruation and fibroids [23], on the other hand, the results indicate a significant negative correlation between PCOS and the level of Insulin (INS) in each of the Insulin Antibody (AIA), Insulin-Like Growth Factor-1 (IGF-1), and ovulation hormone (LH), as their concentration decreases with increased Insulin (INS) and vice versa. This relationship may imply that insulin resistance disrupts the metabolism [24]. Also, the findings in Table-4, confirming that a rise in IGF-1 concentration is an indication that the risk factors for PCOS. The findings revealed a substantial negative link between PCOS and the level of IGF-1 in each of the Insulin Antibody (AIA), Insulin (INS), and BMI, as their concentration increases with decreasing Insulin-Like Growth Factor-1, and vice versa. As it has been shown that high levels of the ovulatory hormone and an increase in its frequency lead to impeding the growth of the follicle and ovulation in addition to that it enhances the secretion of (IGF-1) from the ovaries, which in turn enhances the formation of androgens from (Theca cells) and thus contributes to the formation of cysts in the ovaries [25, 26]. Also, growth factors are able to secrete estrogen hormone from the ovaries and increase the activity of (aromatase) in PCOS women with normal weight. The bioavailability of IGF-1 increases, while it decreases with overweight and obesity [27, 28]. The results, on the other hand, show a substantial positive link between PCOS and the level of IGF-1 in each of the ovulation hormone (LH), estrogen hormone, and progesterone

hormone, as their concentration increases with the increase in the level of IGF-1.

Conclusions

The most common endocrine disorder in women of reproductive age is PCOS (polycystic ovarian syndrome). And the study showed that there is a strong relationship between the impact of the Anti-Insulin Antibody and Insulin-Like Growth Factor on PCOS.

Recommendations

The possibility of adopting the examination of both insulin antibodies (AIA) and insulin-like growth factor-1 (IGF-1) in the diagnosis and treatment of PCOS.

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