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The Role of Diabetes on Polycystic Ovary Syndrome (PCOS)

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ABSTRACT

High estrogen levels may play a role in altering insulin action (insulin resistance), resulting in diabetes with polycystic ovarian syndrome. Both disorders result in a lower incidence of natural conception, often known as estrogen dominance. As a result, the study focused on insulin and its link to Polycystic ovarian syndrome (PCOS) in women. 44 samples were collected from women with polycystic ovarian syndrome, while 46 samples were collected as a control group. The results demonstrated a significant drop in progesterone in women with polycystic ovarian syndrome. The results in this study suggested a relationship between high insulin levels and polycystic ovary syndrome, through a significant positive relationship between insulin and estrogen. While a substantial negative link was found between other clinical parameters and insulin in women with the syndrome, this was due to the high insulin levels and the incapacity of female hormones and anti-insulin antibodies (AIA) to control insulin and blood sugar levels. Finally, the study found a new strong link between diabetes, polycystic ovarian syndrome, and miscarriage via their effects on female hormones.

1. Introduction

One of the most prevalent endocrine disorders affecting girls and women of adulthood is polycystic ovarian syndrome, or PCOS. (Yousif & Al-Jawadi, 2022; Witchell *et al.*, 2019). Studies indicate that in the case of PCOS, an imbalance occurs at the level of the ovulation process. Either the ovary releases mature eggs as it should in its natural state, or the eggs do not mature in the first place, and this can cause many symptoms, including menstrual cycle (Al-Ttaie & Al-Jawadi, 2021; Al-Taie, & Al-Jawadi, 2019)

Some evidence suggests that women with the syndrome may have a defect in insulin action and are more likely to develop insulin-independent diabetes mellitus (IIDM). There are

multiple factors involved in the development of this syndrome that can lead to It leads to infertility in women due to the failure of the follicles to mature and implant the fertilized egg (Hu *et al.*, 2020). Irving F. Stein and Michael Leventhal, two American gynecologists, initially identified the disease in 1935, who called it Stein-Leventhal disease, which is an endocrinopathy disorder that affects an increasing number of women between puberty. And menopause, because it refers to a number of symptoms that appear at the same time, is also known as hyperandrogenic-Anovulation Syndrome (Chang & Dunaif, 2021). In 2012, the National Institute of Health (NIH) approved two of three criteria for identifying and diagnosing anovulation, polycystic ovary syndrome, and hyperandrogenism, which are referred to as the

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Rotterdam criteria using polycystic ovary ultrasound (Lentscher & Decherney, 2021).

Polycystic ovary syndrome is usually diagnosed by specialist doctors when there is a high ratio of ovulation hormone (LH) to follicle-stimulating hormone (FSH), in addition to high concentrations of Androstenedione) in the blood (Saadia, 2020). Ultrasound imaging of the pelvic area may reveal the presence of A number of follicles on one or both ovaries that look like small cysts, but are not necessary for the diagnosis (Rosenfield & Ehrmann, 2016). The condition affects as many as 70% of women, and becomes resistant to insulin, which leads to the accumulation of insulin in the blood and thus prompts the ovaries to increasingly produce androgens, leading to a state of hyperandrogenism (Moggetti & Tosi, 2021). Insulin resistance in polycystic ovary syndrome causes a disorder in multiple mechanisms, including excessive stimulation of IGF-1 receptors, abnormalities in the secretion of pituitary and reproductive hormones, excessive activity of the enzyme that regulates the conversion of (17-hydroxy-progesterone to androstenedione), and also decreased synthesis of growth factor-binding protein. Insulin-like-1 (IGFBP-1) (Lewandowski *et al.*, 2019). The objective of the research is to investigate the impact of diabetes on insulin-resistant women with polycystic ovarian syndrome.

2. Methodology

2.1. Collecting samples

The research was conducted and approved by the author's Institutional Review Board in accordance with the Helsinki Declaration's requirements, between October 1, 2021 and April 20, 2022 in hospital AL-Salaam/ Mosul, Iraq,

The study involved 45 PCOS women with diabetes. Their ages varied from 20 to 43 years old, with 47 women aged 20 to 42 serving as a control group in this study.

During the early follicular phase, on day two or three of the menstrual cycle, blood samples were taken in the morning to measure glucose, insulin, and sex hormones (estrogen E2). The

samples were fasted for 12 hours. Progesterone in both groups on day 13 or 14 of the menstrual cycle, the time of ovulation.

Before the study, samples were given enough time to warm up to the temperature of the room. Then, clinical parameters were then measured using commercial kits (Roche kits) and measured by the Mini Vidas device., France, was utilized to evaluate Insulin Antibody (AIA), Progesterone (P4), estrogen (E2), follicle-stimulating hormone (FSH), and ovulation hormone (LH). Apart from using Roche kits for Insulin INS, Cobas-e411 uses a Spectrophotometer with customized kits to identify glucose. Lastly, the data was analyzed using SPSS software.

2.2. Ethical Approval

The research was conducted and approved by the author's Institutional Review Board.

3. Results and discussion

3.1 The levels of hormonal and biochemical indicators of PCOS with diabetic patients compared to the control group.

The results in Table 1 showed a significant decrease in the concentration of the Progesterone (P4) ng/ml at $P < 0.001$ in PCOS compared with the control group; The results also showed a significant increase in the concentration of Insulin Antibody (AIA), Glucose, Insulin (INS), Ovulation Hormone (LH), Follicle-Stimulating Hormone (FSH), and Esterogen (E2) in patients compared with the control group at $P \leq 0.001$, respectively.

3.2. The correlation of the impact of insulin. on hormonal and biochemical parameters in people with PCOS

Insulin showed in Table 2 a negative relationship with AIA and LH, while the relationship was positive with the rest of the variables, especially with estrogen.

3.3. The incidence of PCOS with regular menstrual cycle

Figure 1. showed the incidence of PCOS with regular menstrual cycle was 74% irregular.

Table 1: The levels of hormonal and biochemical variables of PCOS patients compared with the control group

Variables	Patients Mean ± SD	Healthy Group Mean ± SD	Sig. value
AIA U/ml	5.59 ± 0.3	2.67 ± 0.04	<0.001
Glucose mg/dl	156.21 ± 6.3	73.45 ± 7.3	<0.001
INS μU/ml	14.78 ± 6.7	11.80 ± 3.1	<0.001
HOMA-IR	3.11 ± 1.0	2.12 ± 0.7	<0.001
LH mIU/ml	9.78 ± 2.1	4.26 ± 1.4	<0.001
FSH mIU/ml	7.29 ± 5.2	5.85 ± 1.3	<0.001
E2 pg/ml	90.08 ± 31.1	62.7 ± 30.2	<0.001
P4 ng/ml	0.24 ± 0.2	3.20 ± 0.2	<0.001

Table 2: Correlation of the effect of INS on hormonal and biochemical variables in people with heart attacks

Variables	correlation value (r)	Sig. Value
AIA U/ml	- 0.177	0.544
Glucose mg/dl	0.070	0.59
LH mIU/ml	- 0.104	0.423
FSH mIU/ml	0.152	0.242
E2 pg/ml	0.336	0.008**
P4 ng/ml	0.082	0.532

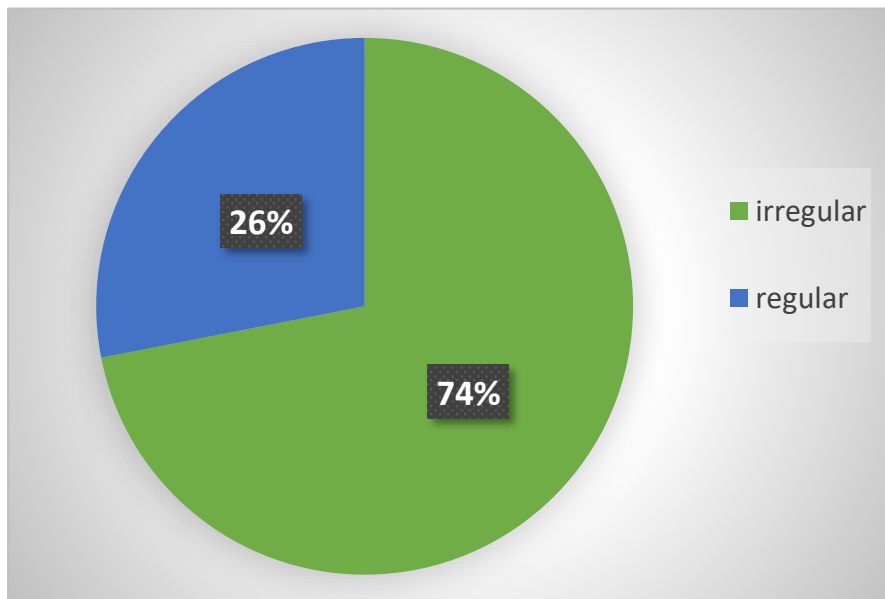


Figure 1. The incidence of PCOS with regular menstrual cycle

3. Results and discussion

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 and becomes more susceptible to an autoimmune reaction because the estrogen hormone stimulates antibodies, which causes the immune

system to send signals that lead to autoimmunity (Merrheim et al., 2020). Increased insulin concentration in women with the syndrome reduces the serum concentration of sex hormone binding globulin (SHBG), which enhances the bioavailability of free testosterone. These women also have an abnormal concentration of gonadotropin-releasing hormone. Gonadotropin Releasing Hormone (GnRH) and androgen

synthesis from the adrenal gland and ovaries which is stimulated by the high level of insulin (Glueck & Goldenberg, 2019). It was also found that increased LH is a hormonal imbalance in women with the syndrome, and this increase may stimulate the production of IGF-1 by theca cells, thus increasing androgen production (Emanuel et al., 2022; Laban et al., 2018). In insulin-resistant PCOS patients, insulin receptors cause excessive serine phosphorylation, which reduces the activity of tyrosine kinase receptors, thus increasing blood glucose levels. Insulin resistance also leads to an increase in the availability of free androgen, and a change in follicular development and granulosa cell function (Granulosa Cell) (Bannigida et al., 2020; Zeng et al., 2019). The reason for the increase in estrogen in women with the syndrome can be attributed to the high percentage of body fat, which in turn can increase its percentage in the body (Mair et al., 2020). While the results indicated a considerable fall in the level of both progesterone hormones in patients. The cause of the deficit of progesterone may be weight gain, which has negative effects on women's fertility through insulin resistance, androgen excess, and chronic ovulation (Yang et al., 2021).

There is a significant association factor, as seen by the results presented in Table 2 between high insulin and the incidence of polycystic ovary syndrome. The findings show a statistically significant positive correlation between insulin and the hormone estrogen. Because estrogen has a large role in controlling the reproductive system, in addition to boosting insulin action, high insulin levels lead to disturbances in the functioning of estrogen and the appearance of symptoms of high levels, such as heavy bleeding during menstruation and fibroids (Zhu et al., 2023; Gupte et al., 2015).

Finally, Figure 1. shows the rate of irregular menstruation in PCOS at 72% with a low level of progesterone, which is an important indicator of women's reproductive health (Mao et al., 2021). Many hormones play an important role in its regularity, and their irregularity is one of the main symptoms of the absence of ovulation, which is accompanied by decreased secretion

and output. of ovarian steroid hormones (Zhou et al., 2022).

4. Conclusions

According to results, higher levels of estrogen in women of reproductive age due to the high insulin levels, especially as they become older, and the study discovered a significant link between diabetes and polycystic ovary syndrome, and the insulin level of patients with PCOS must be measured for the purpose of early diagnosis and treatment.

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