Impact of Insulin Resistance in PCOS (LH / FSH) in A Group of Woman in Baghdad City / Original study

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تأثير مقاومة الأنسولين في متلازمة تكيس المبايض (LH/FSH) لدى مجموعة من النساء في مدينة بغداد

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Abstract

Background: Polycystic ovarian syndrome is an endocrinological disorder influencing ladies, and it is the foremost common cause of menstrual unsettling influence amid the regenerative age. Polycystic ovary disorder (PCOS) is in fact a chronic form of anovulation that is usually observed besides a large spectrum of clinical symptoms and signs. **Objectives**: The study's main goal is to evaluate the hormonal indicators of "PCOS" and insulin resistance and determine how insulin resistance affects these hormones. **Materials and methods**: This study included 130 women, aged 19–38, who were separated into three bunches: 40 women with "PCOs" who were treated with metformin and 50 women with "PCOs" who were not treated with. In expansion, 40 from the control gather. Hormone levels: luteinizing hormone (LH), follicle-stimulating hormone (FSH), insulin resistance, and fasting blood sugar were measured. **Results**: The correlation pattern showed an increasing trend from lower to increased rise of LH compared to FSH. The data reveals that both the untreated and treated groups exhibit significantly elevated levels of fasting blood sugar (FBS), insulin, and insulin resistance (IR) when compared to the control group. However, the untreated group displays the highest levels for all these parameters. **Conclusions**: This study shows a significant association between insulin resistance levels and the LH proportion in ladies with PCOS. The studied parameters may play an important role in the evaluation of therapeutic responses in POCS women in Baghdad City.

Keywords: Insulin Resistance, PCOS, LH, FSH, Fasting Blood Sugar, Metformin, BMI.

Abbreviations

PCOS: Polycystic ovary syndrome

LH: luteinizing hormone

FSH: Follicle-Stimulating Hormone

FBS: fasting blood sugar

IR: insulin resistance

BMI: body mass index

SHBG: sex hormone-binding globulin

المستخلص

الخلفية: متلازمة تكيس المبايض هي اضطراب غددي يصيب النساء وهو السبب الأكثر شيوعًا لاضطرابات الدورة الشهرية في سن الإنجاب. متلازمة تكيس المبايض هي في الواقع شكل مزمن من انقطاع التبويض والذي يُلاحظ عادةً إلى جانب مجموعة كبيرة من الأعراض والعلامات السريرية. **الأهداف:** تركز الدراسة على تقييم العلامات الهرمونية لمتلازمة تكيس المبايض ومقاومة الانسولين ومعرفة تأثير مقاومة الانسولين على هذه الهرمونات. **المواد والطرائق العمل:** شملت هذه الدراسة 130 امرأة تتراوح أعمارهن بين 19 و38 عامًا، تم تقسيمهن إلى ثلاث مجموعات: 40 امرأة مصابة بمتلازمة تكيس المبايض تم علاجهن بـ (الميتفورمين) و50 امرأة مصابة بمتلازمة تكيس المبايض لم يتم علاجهن بـ (الميتفورمين). بالإضافة إلى ذلك، مثلت المجموعة الضابطة 40 امراة. قيست مستويات الهرمونات و مقاومة الآنسولين و سكر الدم الصائم وLH.FSH **النتائج:** أظهر نمط الارتباط اتجاهًا متزايدًا من ارتفاع منخفض إلى متزايد في LH مقارنة بـ FSH تكشف البيانات أن كل من المجموعتين غير المعالجة والمعالجة تظهر مستويات مرتفعة بشكل ملحوظ في سكر الدم الصائم (FBS) والأنسولين ومقاومة الأنسولين (IR) عند مقارنتها بمجموعة التحكم. ومع ذلك، فإن المجموعة غير المعالجة تظهر أعلى المستويات لجميع هذه المعايير.

الاستنتاجات: تظهر هذه الدراسة ارتباطًا مهمًا بين مستويات مقاومة الأنسولين ونسبة LH لدى النساء المصابات بمتلازمة تكيس المبايض. قد تلعب المعايير المدروسة دورًا مهمًا في تقييم الاستجابة العلاجية لنساء POCS في مدينة بغداد.

هذا البحث يكتشف ارتباطًا إيجابيًا جديرًا بالملاحظة بين مستويات مقاومة الأنسولين ونسبة LH لدى النساء المصابات بمتلازمة تكيس المبايض.

الكلمات المفتاحية: مقاومة الأنسولين، متلازمة تكيس المبايض، LH، FSH، سكر الدم الصائم، الميتفورمين، مؤشر كتلة الجسم.

Introduction

Polycystic ovary syndrome (PCOS) an endocrinologic disorder among women of reproductive age with a predominance of 4-18% (Ding, et al., 2018), although infertility is a major problem in females with PCOS, hormone disorders including menstrual abnormalities (oligomenorrhea or amenorrhea), chronic anovulation and hyperandrogenism(resulting in androgenic alopecia, acne, and hirsutism) are also common problems in these women (Zhang, *et al*., 2018).

Polycystic Ovary Disorder (PCOS) could be a heterogeneous clutter characterized by constant ovulatory dysfunction and hyperandrogenism. It is considered as the foremost common endocrinological issue influencing ladies, and the foremost predominant cause of their menstrual abnormalities amid the regenerative age (Saadia, *et al*., 2020).

Polycystic Ovary Disorder could be a therapeutic condition characterized by a collection of symptoms that negatively impact a woman ovulatory function and ovarian morphology (Singh, *et al*., 2023). The present condition was initially characterized in 1935 (Witchel, *et al*., 2019), and it is typified by persistent anovulation, a polycystic ovary, female sterility, menstrual irregularities, hirsutism, hyperandrogenism, and excessive weight gain (Singh, *et al*., 2023). The emergence of pathological or atypical cysts, including polycystic ovary syndrome (PCOS) cysts, may lead to distressing and uncomfortable symptoms. A diagnosis of Polycystic Ovary Syndrome requires that a woman manifest at least two of the previously delineated symptoms (Rasquin, *et al*., 2022).

Insulin resistance is present in many, if not most, women with PCOS (Amisi, 2022). Although the mechanism of insulin resistance in PCOS remains

incompletely understood, the underlying defect is reported to occur within the post-receptor phosphatidylinositol 3-kinase (PI3K) insulin pathway that mediates the metabolic effects of insulin. Other factors may also contribute towards the establishment of insulin resistance in women with PCOS.

Follicle stimulating hormone, commonly abbreviated to FSH, belongs to the 'gonadotropin' group of hormones (Orlowski & Sarao, 2022).

The treatment of PCOS is primarily symptomatic rather than pathophysiological. The central component of the disorder is thought to be a neuroendocrine clutter, as prove by raised LH/FSH proportions in PCOS ladies, particularly in ladies with destitute PCOS (Pratama, *et al*., 2022).

As a reaction to the rise in FSH levels amid the early follicular stage, there will be a expansion of granulosa cells. This rise within the number of granulosa cells will cause a concurrent rise in FSH receptors on the cells. The expanded FSH levels permit the granulosa cells to deliver estradiol, which initiates LH receptors on granulosa cells as well. With LH receptors presently display, the granulosa cells will deliver little sums of progesterone and 17hydroxyprogesterone. The progesterone discharged by the granulosa cells controls granulosa cell expansion and eventually moderates follicular development (Monis & Tetrokalashvili, 2022).

Based on a 28-day cycle, the follicular stage measures from the primary day of feminine cycle (day 0) until the starting of ovulation (day 14). When the past menstrual cycle completes, and the corpus luteum breaks down, the levels of estrogen, progesterone, and inhibin A will diminish. This chain of occasions will cause positive criticism to the hypothalamus and front pituitary, and a ensuing pulsatile discharge of GnRH and FSH into circulation. This increment in FSH will invigorate the granulosa cells of the ovaries to

enroll a few follicles from each ovary. These follicles will total development, and as it were one Graafian follicle will go through ovulation amid that cycle. The increment in FSH too fortifies the emission of Inhibin B by the granulosa cells. Inhibin B will in the long run limit the emission of FSH toward the conclusion of the follicular stage. Inhibin B levels will be most elevated amid the LH surge some time recently ovulation, and will rapidly decrease off after (Reed & Carr, 2018). The goals of the study are focuses on evaluating the hormonal markers of polycystic ovary syndrome and insulin resistance and determining the effect of insulin resistance on these hormones.

2.Materials and methods

2.1 Patients and samples

This study included 130 female aged 19 to 38 years, categorized into three cohorts: 40 women with PCOs treated (metformin) and 50 women with PCOs untreated, and 40 control. Female data encompassed various factors, including age, length, weight.

Samples collection: collected 5 ml blood from each woman attended Kamal Al-Samarrai Hospital for Infertility and Baghdad Medical City with PCOs, and the same volume of blood from the control group, then transferred into gel tubes, all samples were appropriately labeled, sent to the laboratory using dry-ice packs to maintain low temperatures.

Inclusion criteria: Based on the gynecologist's diagnosis, a serum sample from polycystic ovary syndrome female was collected.

Exclusion criteria: pregnant woman

2.2 Determination of Fasting Blood Sugar (FBS) (mg/dL):

The blood sample was prepared after the centrifugation process, and only the serum was taken. An amount of 0.5 ml from serum was placed in the cuvette to read the absorption rate. The absorbance was measured at 505 nm. Serum fasting blood sugar (FBS) ≥120 mg/dl was decided by utilizing the Mindray BA-88A machine, a semi-automated organic chemistry analyzer outlined to perform a wide extend of biochemical tests. FBS: (75_126 mg/dl), (4.1_6.1 mmol/l). (Ambade, *et al*., 1998).

2.3 Determination of Fasting Insulin (µU/mL):

Using the Roche Kit of the Cobas equipment 0.5 ml of serum was taken and placed in the device. COBAS INTEGRA 400 plus analyzer, a fully automated device that uses more than 140 applications for all types of sample matrices, was used to measure serum fasting insulin (Dahman, *et al.,* 2021).

2.4 Determination of HOMA-IR:

A measurement of blood sugar is made. Together with the insulin level test, the woman's degree of insulin resistance is then determined using the equation.

Insulin Resistance = [(fasting glucose mg/dL) x (blood insulin Î¼U/mL)] / 405 or

Insulin Resistance = [(fasting glucose mmol/L) x (blood insulin Î¼U/mL)] / 22.5. The optimal insulin sensitivity of HOMA-IR is less than 1, while levels above 1.9 signal early insulin resistance, and a value of 2.5 or above is taken as an indicator of IR in females (Cheang, *et al*., 2019).

2.5 Measure Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH):

Levels were determined on cycle day 2 to secure normality of ovarian functions. Hormonal measurements were done by using Mini Vidas (bio Merieux, France and U.S.A.) (Zhao, *et al*., 2023).

2.6 The statistical analysis:

Performed using IBM SPSS statistics software (version 26.0). Results analyzed using Variation-ANOVA and expressed as mean ± standard error. The p-value was used to determine level of statistical significance, with $p \leq 0.05$ or $p \leq 0.0001$ being statistically significant.

3. Results

3.1 Demographical characteristic of the study groups

The results shown highly significant (P-value ≤0.0001) by observed the most cases of PCOs were obese and overweight BMI (Kg/m^2) among the untreated (not taken metformin treatment) groups than (taken metformin treatment) with 18/50 (51.4%),21/50 (34.4%)00/11 ، (26.2%),16/40 (45.7%) respectively.

The results of the current study recorded the number of untreated (not taken metformin treatment) cases which diagnosed with PCOs were 35 out of 50 (41.7%) at the age groups (19-28) years, while the number of treated (taken metformin treatment) cases which diagnosed with PCOs were 25 out of 40 (29.8%) at the age groups (19-28) years. The results about moreover archived the number of untreated (not taken metformin treatment)

cases which analyzed with PCOs were 12 out of 50 (30%) versus 13 out of 40 cases of treated (taken metformin treatment) were at the age bunches (29-38) a long time, Whereas the less cases of PCOs of both untreated and treated cases were recorded at the age bunches 38< were 2 (33.3%),3 (50%) separately, measurably these contrasts were non-significant (P-value=0.66) as illustrated in Table (1).

Table (1): Characterization of Age range (years) and BMI (Kg/m^2) among cases (treated, untreated) and control group

Variable	Category	Treated (n=40)	Untreated (n=50)	Control (n=40)	Total	P value	Sig.
Age range (Years)	(19-28)	25 (29.8%)	35 (41.7%)	24 (28.6%)	84 (100.0%)	0.66	N.S
	(29-38)	13 (32.5 %)	12 (30.0%)	15 (37.5%)	40 (100.0%)		
	<38	2 (33.3%)	3 (50.0%)	1 (16.7%)	6 (100.0%)		
Total		40 (30.8%)	50 (38.5%)	40 (30.8%)	130(100.0%)		
BMI (Kg/m^2)	Normal weight	8 (23.5%)	11 (32.4%)	15 (44.1%)	34 (100.0%)	0.001	H.S
	Overweight	16 (26.2%)	21 (34.4%)	24 (39.3%)	61 (100.0%)		
	Obese	16 (45.7%)	18 (51.4%)	1 (2.9%)	35 (100.0%)		
Total		40 (30.8%)	50 (38.5%)	40 (30.8%)	130(100.0%)		

The results of this study showed the mean age of PCOs female whose treated and untreated were 28.20±4.45, 26.76±5.94 respectively in compared with control groups were 27.57±4.70, These differences had P-value=0.45.

The results of the current study observed the mean of BMI (Kg/m^2) of treated groups were higher than untreated group with30.40±5.68, 29.67±6.26 respectively in compared with control groups were 25.17±2.45, These differences had P-value ≤0.0001 as arranged in Table (2).

Table (2): Comparative the mean levels of Age (Years) and BMI (Kg/m²) among cases (Treated, Untreated) and Control groups (n=40)

Test	Groups	M±SD	SE	P-value
Age (Years)	G1-Treated (n=40)	28.20±4.45	0.70	0.45
	G2-Untreated (n=50)	26.76±5.94	0.84	
	G3- Control (n=40)	27.57±4.70	0.74	
BMI (Kg/m²)	G1-Treated (n=40)	30.40±5.68	0.89	≤0.0001
	G2-Untreated (n=50)	29.67±6.26	0.88	
	G3- Control (n=40)	25.17±2.45	0.38	

3.2 Comparative analysis of the average levels of fasting blood sugar (F.B.S), insulin, and Insulin Resistance (IR) among three groups.

Table (3) showed a comparative analysis of the average levels of fasting blood sugar (F.B.S), insulin, and insulin resistance (IR) across three groups: treated (G1), untreated (G2), and control (G3).

The p-values for comparisons between groups (G1&G3, G2&G3, G1&G2) are all ≤0.0001, indicating highly significant differences (H.S) in F.B.S levels among the groups. The ANOVA p value is also ≤0.0001, confirming that at least one group differs significantly from the others. Similar to F.B.S, the p-values for comparisons between groups are all ≤0.0001, indicating significant differences in insulin levels. The ANOVA p-value is also ≤0.0001. as well as, the p-values for comparisons are ≤0.0001, indicating significant differences in IR levels among the groups. The ANOVA p-value is ≤0.0001. The data reveals that both the untreated and treated groups exhibit significantly elevated levels of fasting blood sugar (F.B.S), insulin, and insulin

resistance (IR) when compared to the control group. However, the untreated group displays the highest levels for all these parameters.

Table (3): Comparative the mean levels of F.B.S(mg/dl) Insulin (MI/UL) and IR among cases (Treated, Untreated) and control

Test	Groups	M±SD	G1&G3		G2&G3		G1&G2	
			P-value	Sig.	P-value	Sig.	P-value	Sig.
FBS (70-120)	G1-Treated (n=40)	96.32±9.35	≤0.0001	H.S	≤0.0001	H.S	≤0.0001	H.S
	G2-Untreated (n=50)	109.20±6.61						
	G3- Control (n=40)	79.72±6						
ANOVA P-value		≤0.0001 (H.S)						
Insulin (2-25)	G1-Treated (n=40)	7.20±3.35	P-value	Sig.	P-value	Sig.	P-value	Sig.
	G2-Untreated (n=50)	9.95±3.87	≤0.0001	H.S	≤0.0001	H.S	≤0.0001	H.S
	G3- Control (n=40)	3.17±0.97						
ANOVA P-value		≤0.0001 (H.S)						
IR (0-1.2)	G1-Treated (n=40)	1.71±0.83	≤0.0001	H.S	≤0.0001	H.S	≤0.0001	H.S
	G2-Untreated (n=50)	2.70±1.10						
	G3- Control (n=40)	0.6279±0.20						
ANOVA P-value		≤0.0001 (H.S)						

3.3 Comparative the mean levels of FSH and LH between case.

The results of this study showed that the mean levels of FSH were normal in range when compared with normal range (3-11 mg/dl) with little differences, statistically these differences were highly significant (P-value ≤0.0001) as arranged in Table (4). The results of this study also showed there were a highly differences (P-value ≤0.0001) in the levels of FSH between treated and control groups (G1&G3) and between untreated and control (G2&G3) with (P-value ≤0.0001) , While there was a non-significant differences (P-value=0.089) in the levels of FSH between treated and untreated groups (G1&G2).

The mean levels result of LH showed that G1 compared to G3: There is a p-value of 0.09, showing that there is no significant distinction (N.S.) between the treated and control groups.

• In the comparison of G2 and G3, the p-value of ≤0.0001 shows a highly significant difference (H.S.) between the untreated and control groups, with the untreated group showing higher LH levels.

G1 compared to G2: A p-value of 0.01 shows a significant distinction between the treated and untreated groups, with the untreated group showing elevated LH levels.

Table (4): Comparative the mean levels of FSH and LH between cases (n=90) and Control (n=40)

Test	Groups	M±SD	G1&G3		G2&G3		G1&G2	
			P-value	Sig.	P-value	Sig.	P- value	Sig.
FSH mg/dl (3-11)	G1-Treated (n=40)	5.71±1.46	≤0.0001	H.S	≤0.0001	H.S	0.089	N.S
	G2-Untreated (n=50)	6.20±1.25						
	G3- Control (n=40)	7.36±1.38						
ANOVA P-value		≤0.0001 (H.S)						
			P-value	Sig.	P-value	Sig.	P- value	Sig.
LH mg/dl (1-12)	G1-Treated (n=40)	9.65±2.60	0.09	N.S	≤0.0001	H.S	0.01	S
	G2-Untreated (n=50)	11.07±2.99						
	G3- Control (n=40)	8.64±1.83						
ANOVA P-value		≤0.0001 (H.S)						

3.4 Comparative the mean levels of FSH and LH between cases and control according to BMI (Kg/m^2) score.

The results of this study (Table 5) showed that there was a highly significant differences (P-value = 0.001) in the levels of Insulin among female groups whose untreated with metformin with high levels among obese groups (12.01±3.31) than overweight and normal weight groups with (9.81±3.72, 6.82±2.94) when comparing with the levels with control groups. While there was a non-significant difference (P-value ≥0.05) in mean levels of FBS (mg/dl) between the female groups whose treated and those whose untreated with metformin in comparing with control groups when classified according to BMI scores.

Also there was a non-significant difference (P-value ≥0.05) in mean levels of insulin between the female groups whose who treated with metformin when classified according to BMI scores.

Table (5): Comparative the mean levels of FBS, Insulin, IR, FSH and LH between cases and control according to BMI (Kg/m^2) score.

Test	Groups	BMI (Kg/m^2) score			P-value	Sig.
		Normal weight	Overweight	Obese		
		M±SD	M±SD	M±SD		
FBS (mg/dl)	Treated	99±7.48	94.75±8.72	96.56±10.89	0.58	N.S
	Untreated	108.90±5.61	108.04±6.35	110.72±7.48	0.46	N.S
	Control	78.93±6.30	80.16±6.01	81.0±0	0.81	N.S
Insulin	Treated	6.43±3.27	7.17±3.60	7.60±3.28	0.73	N.S
	Untreated	6.82±2.94	9.81±3.72	12.01±3.31	0.001	H.S
	Control	2.85±0.69	3.38±1.09	3.0±0	0.25	N.S
IR	Treated	1.58±0.81	1.67±0.86	1.82±0.85	0.77	N.S
	Untreated	1.84±0.82	2.63±1.04	3.30±0.99	0.001	H.S
	Control	0.55±0.15	0.67±0.23	0.60±0	0.25	N.S
FSH	Treated	6.13±1.82	5.93±1.62	5.27±1.0	0.29	N.S
	Untreated	5.99±1.26	6.50±1.30	5.99±1.19	0.38	N.S
	Control	7.56±1.22	7.19±1.48	8.50±0	0.57	N.S
LH	Treated	8.52±1.90	9.54±3.05	10.33±2.32	0.27	N.S
	Untreated	9.83±2.26	10.87±2.85	12.06±3.34	0.14	N.S
	Control	8.83±1.50	8.65±1.98	5.70±0	0.26	N.S

4. Discussion

PCOS is one of the most causes of infertility. PCOs, oligo-anovulation, and hyperandrogenism are among the diagnostic criteria, but a lot of PCOS-afflicted women are also overweight or obese. The management of symptoms and reproductive results are both impacted by adiposity, which has a significant impact on specific PCOS phenotypes (Cena, *et al*., 2020).

The results shown highly significant (P-value ≤0.0001) by observed the most cases of PCOs were obese and overweight BMI (Kg/m^2) among the untreated (not taken metformin treatment) groups than (taken metformin treatment) with 18/50 (51.4%),21/50 (34.4%)00/11 ، (26.2%),16/40 (45.7%) respectively .Thus agreed with (Jensterle, *et al*., 2020) who metformin made strides the metabolic profile of ladies with PCOs over a cruel follow-up of 36.1 months, especially in HDL cholesterol, diastolic blood weight and BMI. In expansion, ladies with PCOs who too had the metabolic clutter at standard showed up to gather more metabolic benefits from metformin.

Findings suggest that affront resistance could be a key highlight of polycystic ovary disorder (PCOS) and may increment the hazard of cardiovascular disease. Because of insulin resistance, metabolic disorder is more predominant in ladies with PCOS than in ordinary ladies. Metformin progresses the metabolic profile in PCOS in short-term thinks about. Within the Indian consider assessed the long-term impact of metformin on metabolic parameters in ladies with PCOS amid schedule care without a controlled count calorie. Metabolic chance variables were compared some time recently and after metformin treatment (Shahebrahimi, *et al*., 2016). Improvements in body mass file were watched. The predominance of metabolic disorder diminished from 34.3% at first to 21.4% (p = 0.0495). The BMI lessening

direction amid metformin treatment was essentially more articulated in PCOS ladies with metabolic disorder at standard, compared with those without metabolic disorder (p = 0.0369 for interaction). In conclusion, metformin progressed the metabolic profile of PCOS ladies over 36.1 months, especially in BMI (Akhtar, *et al*., 2021). Other studies observed that metformin with way of life alteration driven to the lessening of BMI. Most of the considers found comparative comes about and few considers moreover found that metformin diminished affront resistance indeed without decreasing BMI in PCOS (Melin, *et al*., 2023).

The results were similar to those of the two Iraqi researchers (Alsaadi and Mohamad, 2019). There was a statistically significant difference ($P < 0.05$) in body mass index between women with polycystic ovary syndrome and control ladies. The predominance of overweight and corpulence was also significantly higher in women with polycystic ovary syndrome than in matched control women.

Being the most prevalent endocrine disorder in women of reproductive age.

It is commonly acknowledged that adipose tissue functions as an active endocrine organ, generating and secreting "adipokines," which are biologically active chemicals. Adipokines play a role in the control of several homeostatic processes, including the regulation of insulin sensitivity, atherosclerosis, inflammation, and energy metabolism. Adipose tissue alters structurally and functionally with obesity, causing high blood sugar, high cholesterol, high leptin levels, and persistent low-grade inflammation. It appears that women with PCOS experience similar changes in their adipose tissue (Calcaterra, *et al*., 2021).

The negative effects of PCOS on metabolism and reproduction are further exacerbated by obesity. Adipogenesis and lipolysis are both boosted by obesity's increased insulin resistance and compensatory hyperinsulinemia, which also boosts adipogenesis. Obesity upregulates the synthesis of ovarian androgen, which in turn makes thecal cells more sensitive to LH activation and intensifies functional ovarian hyperandrogenism. There is a vicious feedback cycle between obesity and inflammatory adipokines, which promote hyperinsulinemia and, in turn, obesity (Glueck & Goldenberg, 2019).

Table (1) showed comparison between treated and untreated PCOS groups showed a slight, but not statistically significant, increase in mean age in women participating in the study, respectively (84 (100.0%), 40 (100.0%), 6 (100.0%). This marginal difference, as indicated by the p-value of 0.66, suggests that while there may be a trend towards higher levels of age (19–28) in PCOS female, it is not large enough to draw definitive conclusions. This finding is consistent with some studies suggesting that environmental factors such as endocrine disruptors may be associated with PCOS, but more robust and larger studies are needed to confirm any significant associations (Kshetrimayum, *et al.,* 2019). This results agreed with (Jozkowiak, *et al.,* 2022) polycystic ovary disorder (PCOS) is the foremost common heterogeneous endocrine clutter among ladies of regenerative age. The pathogenesis of PCOS remains tricky; in any case, there's prove proposing the potential commitment of hereditary intelligent or inclinations combined with natural components (Jozkowiak, *et al*., 2022).

As shown in Table (2) the results can explained as Jozkowiak, said in their study that the prognosis of IR is commonly associated with the excessive production of inflammatory cytokines such as (IL-8, IL-10, IL-12) and acute-phase

proteins such as CRP (Peña, *et al*., 2020). Polycystic ovarian disorder (PCOS) is one of the promptly perceived endocrine organ sicknesses in ladies, being overweight, and feebleness. Long-term, low-grade irritation has risen as a vital figure driving to PCOS. In Indian ponder they found a rise in glucose levels may invigorate oxidative stretch and alarming response from mononuclear cells (MNC) of females with PCOS, which regularly don't rely on fat. This is often required since MNC-derived macrophages are the major source of cytokine blend in enormous fat tissue and additionally energize adipocyte cytokine generation. In outline, information un cover the significant dangers of affront resistance in stout individuals who are enduring from PCOS. The discoveries of this particular lesson shown that people with the customary PCOS phenotype had weight and higher affront levels and affront resistance, ignoring the nonappearance of BMI contrasts from other phenotypes (Purwar & Nagpure, 2022).

Besides, smothered levels of serum adiponectin in ladies with PCOS compared with BMI-matched control ladies (illustrated in a huge meta-analysis on>3400 subjects) may assist contribute towards the foundation of affront resistance in PCOS. The part of tall atomic weight adiponectin in PCOS remains not completely caught on and ought to shape a center for future investigate as there may be suggestions for treatment, as proposed by a later consider in a rat show of PCO (Barber & Franks, 2020).

An inadequate cellular response to insulin activity is referred to as insulin resistance, which is considered an important aspect of PCOS multisystem pathophysiology. Insulin resistance exacerbates hyperandrogenism and the resulting hyperinsulinemia increase ovarian androgen synthesis while decreasing hepatic sex hormone-binding globulin (Greenwood & Huddleston, 2019).

Different clinical phenotypes of PCOS carry diverse metabolic dangers, and the classic and ovulatory phenotypes are characterized by IR. Hyperandrogenemia is caused by IR and hyperinsulinemia, which have the impact of boosting LH's effect on ovarian androgen union. Insulin and androgens both block Sex hormone-binding globulin (SHBG) secretion, which raises free and bioactive androgen levels and exacerbates clinical androgen excess. Additionally, IR plays a significant role in the development of metabolic syndrome and cardiovascular disease in PCOS women (Polak, *et al*., 2016).

In women with PCOS, IR stimulates the release of insulin from pancreatic cells and encourages adipose tissue mobilization alongside an elevation of hepatic production. All these actions cause a rise in plasma-free fatty acid (FFA) which in turn impairs glucose transport function by the inactivation of major enzymes such as dehydrogenase pyruvate (PDH) (Ding, *et al*., 2021).

Sex hormone-binding globulin (SHBG) is the most official protein for testosterone, and it is the unbound testosterone (moreover called free testosterone) that acts on target tissues. Affront is accepted to cause a rise in circulating levels of free testosterone by two correct components: to begin with, by empowering ovarian biosynthesis and emission of testosterone, and, moment, by straightforwardly inhibiting hepatic production of SHBG (Mayer, *et al*., 2015).

Higher levels of circulating insulin, contribute to hyperandrogenemia in women with PCOS which in turn promotes the production of ovarian androgen and suppresses the development of sex hormone-binding globulin. This scenario of events could be one mechanism underpinning the increased risk of T2D in women with hyperandrogenemia in PCOS. An alternative mechanism may involve elevated levels of free testosterone, which could exacerbate insulin resistance (Persson, *et al*., 2021).

Our result in Table (4) the mean levels of FSH were normal in range when compared with normal range (3-11 mg/dl) with little differences, statistically these differences were highly significant (P-value ≤0.0001). The normal gonadotrophin axis is disturbed in women with PCOS, thus increasing LH levels and decreasing FSH levels, leading to an inversion of the LH/FSH ratio (Balen, *et al*., 2003).

However, Saadia's study failed to show any significant association between BMI and serum hormone levels in women with PCOS including LH, FSH, and LH/FSH ratio.(Saadia, 2022). Obesity, insulin resistance, and dyslipidemia are comorbidities associated with PCOS and have been found to be associated with the LH/FSH ratio in a nationally representative sample of postmenopausal women in the United States (Beydoun, *et al*., 2012).

At level of LH and FSH our result agreed with Malini and Roy study that said there is relationship of insulin to LH and testosterone was positive and significant ($p<0.05$) within the whole PCOS bunch and in five PCOS subcategories with expended LH rise (i.e. 1.3, 2, 3, 4 & 5 times of LH rise in connection to FSH levels in each gather individually) (Malini & Roy, 2021).

This consider found noteworthy affiliations between affront levels or HOMA-IR and the LH proportion as appeared in Table (3). This contrasts with a ponder by Pratama, *et al*., which appeared a negative relationship between affront resistance and LH levels or the LH/FSH proportion (Pratama, *et al*., 2024).

About the result shown in table (5) we can say there are certainly some limitations to this study. First, when considering the outcomes for overweight/obese patients, it should be noted that these were exploratory analyses of subsequent subgroups of the original trial and were not pre-specified in the study designs, and therefore, the results should be treated with caution.

Second, the number of patients was relatively small and may have introduced statistical bias. It is worth noting that a personalized protocol, similar to the approach used in treating other medical conditions, may lead to better outcomes. Therefore, future research should focus on conducting additional studies with longer follow-up periods.

5. Conclusion

The factors under study might be crucial for assessing the therapy response of PCOS women in Baghdad City.

Remarkably, this study discovered a strong positive correlation between the LH and insulin resistance levels in PCOS-afflicted women.

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