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Relation of Leptin to Insulin and Other Sexual Hormones to Patient with Pcos

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Background: *PCOS considered as the most common endocrine disorder that affect women in reproductive-agewith key features of irregular menstruation, hyper androgenism, and polycystic ovaries. The major abnormality that is associated Withpcos is the insulin resistance (IR), present in about 50-70%. Insulin resistance(IR) considered an important risk factor for the development of the metabolic syndrome in women with PCOS . Insulin resistance and compensatory hyperinsulinemia can be triggered by obesity with visceral fat accumulation. Fat tissue secretes bioactive cytokines and adipokines, including leptin. Some evidence suggested an association between dysregulated expression of leptin and the onset of obesity-related pathologies including PCOS. Leptin is known to have many interactions in the female reproductive system.*

Objectives: *To study the role of leptin in follicular fluid and blood of PCOS patients.Correlation of follicular fluidleptin with serum insulin and other hormones.Correlation of follicular fluid hormones with serum hormones.Correlation of follicular fluid hormones with insulin.*

Patients and Method: *70 women were involved in this study , 35 as healthy control group and 35 patients with PCO.A full history was taken from all participant in the study. A thorough physical examination was done to all patients and control groups. In addition body mass index(BMI) was measured for all as well as measurement of hip and waist circumference to estimate hip/waist ratio. 5ml of blood was aspirated from patients and control groups and centrifuged for 5 min at(3000 rpm), serum was aspirated to measure Luteinizing hormone(LH),Folliculer stimulating hormone(FSH),Estrogen and testosterone.In addition to estimation of leptin and insulin .Follicular fluid was taken from all participant for which estimation of leptin and insulin was done. All patients has done abdominal and vaginal Ultrasound by a specialist gynecologist to prove the diagnosis of PCOS.*

Result: *Results shows that there was no significant difference between patient and control regarding fasting blood sugar which was (p=0.875), insulin in serum was(p=0.296), insulin in follicular fluid was (p=0.285), while significant difference were observed between patient and control regarding leptin level in serum which was (p=0.03)leptin in follicular fluid was (p=0.01) Significant difference was observed in LH level(P=0.001) in PCOS women and the control group.The mean LH level in PCOS women was 5.1 ± 3.1 mIU/ml and in control group was 3.06 ±1.17 mIU/ml.There was no significant difference in mean of FSH level in PCOS and control group. LH/FSH ratio in patient with PCOSwas ≤2 in about 85% of them.*

Conclusion: *From this study we can conclude that significant inverse relation was found between serum insulin and serum leptin in both patient and control group. non significant difference was found in FSH, BMI between the two groups.*

Keywords: *PCOS, Leptin, Insulin Resistance.*

I. Introduction

PCOS considered as the most common endocrine disorder that affect women in reproductive-age (affecting 4-10%), with key features of irregular menstruation, hyper androgenism, and polycystic ovaries.Systematic screening of women according to the National Institutes of Health (NIH) diagnostic criteria estimated that 4–10% of women of reproductive age suffer from PCOS(1) . Although it was previously considered as a disorder of adult women, recent evidence suggests that PCOS is a lifelong syndrome, manifesting since prenatal age. According to the Rotterdam diagnostic criteria, the prevalence of PCOS in adolescents varies between a minimum of 3% and a maximum of 26%(2) . However, the prevalence of the disease in children is still considered unknown (3). The majority of women with PCOS presents some degree of insulin resistance, even non obese. The resulting hyperinsulinemia causes an increase in the production of androgens as in the biologically active state(4).The major abnormality that is associated with pcos is the insulin resistance (IR), which increase the risk of type 2 diabetes. IR is present in about 50-70 percent of PCOS women independently of obesity.(IR) considered an important risk factor for the development of the metabolic syndrome in women with PCOS. It is known that IR progresses towards the development of compensatory hyperinsulinemia, which drives hyperandrogenemia in these women. Insulin resistance and compensatory hyperinsulinemia can be triggered by obesity with visceral fat accumulation.

Fat tissue secretes bioactive cytokines and adipokines, including adiponectin, leptin, and resistin, Some evidence suggested an association between dysregulated expression of leptin and the onset of obesity-related pathologies including PCOS.Long-term hyperinsulinemia has been shown to increase both expression of the ob gene and leptin, which is its product, both in-vivoand in-vitro. This may show some kind of interaction between leptin and insulin which may prove to be important. Leptin is known to have many interactions in the female reproductive system(10).Polycystic ovaries develop when excessive amounts of male hormones (androgens), particularly testosterone are produced by the affected ovary, this occur by either the release of high levels of insulin in the blood, excessive release of luteinizing hormone by the anterior pituitary in women who had sensitive ovary to this stimulus or decrease levels of sex-hormone binding globulin (SHBG) resulting in elevated level of free androgens . The follicular development occur from primordial follicles but due to the disturbed ovarian function this development has stopped at an early antral stage. The follicles appearing as a 'string of pearls' along the ovarian periphery on ultrasound examination

II. Patient And Method

70 women were involved in this study , 35 as healthy control group and 35 patients with PCO.A full history was taken from all participant in the study. A thorough physical examination was done to all patients and control groups. In addition body mass index(BMI) was measured for all as well as measurement of hip and waist circumference to estimate hip/waist ratio. 5ml of blood was aspirated from patients and control groups and centrifuged for 5 min at(3000 rpm), serum was aspirated to measure Luteinizing hormone(LH),Folliculer stimulating hormone(FSH),Estrogen and testosterone.In addition to estimation of leptin and insulin .Follicular fluid was taken from all participant for which estimation of leptin and insulin was done. All patients has done abdominal and vaginal Ultrasound by a specialist gynecologist to prove the diagnosis of PCOS.spss version 20 and excel 2010 was used to study the statistics, chi square used to determine association between two characteristics, with t-test to define the difference between two characteristics mean and correlation were done to assign the statistical linear association between two numerical variables ,p value ≤ 0.05 considered as significant.

III. Results

Seventy subjects were included in this study (35 patient and 35 control), their age ranged from 15-45 years.the mean age of patient were (28.77. ± 5.57) and in control were (31.54±7.20). No significant difference were found between patient and control regarding PCV (p=0.962). The mean PCV in patient group was37.85 ± 5.70L/L and in control group was37.80 ± 2.88 L/L. It was observed that the mean height In patient group were161±5.75 cm and 161.73±5.67 cm in control group with no significant difference between them. The observed mean weight were 78.09±16.15 Kg in patient, 77.02±16.3Kg in control and no significant difference between them.The BMI index in patient was 30.186±5.613cm^2/kg versus 29.330±5.31cm^2/kg in control**.**
The table will illustrate the different mean of the sex hormones which was measured in the study subjects**.**

Table 1. Shows Different Sex Hormone Levels Among Patient With Pcos And Control

parameters	Patients group(N=35) mean±SD	Control group(N=30) mean±SD	P VALUE
FSH mIU/ml	5.78±2.06	6.22±1.83	0.38
LH mIU/ml	5.16±3.13	3.07±1.17	0.001*
Estrogenng/ml	2585.33±8.72	577.65±648.30	0.005*
Progesteronng/ml	0.42±0.51		
Testosteroneng/ml	5.44±8.81		
Prolactinng/ml	19.69±8.72		

Table 3.5: Comparison between patient and control regarding insulin in serum and follicular fluid leptin

Parameters	Patients group(N=35) mean± SD	Control group(N=30) mean± SD	P VALUE
FBS mmol/l	5.16 ± 0.80	5.08 ± 1.86	0.875
Insulin in serum ng/ml	18.38 ± 10.29	22.05±22.36	0.296
Insulin in follicular fluidng/ml	7.64 ± 8.04	9.80 ± 9.90	0.285
Leptin in serum ng/ml	87.51 ± 19.91	92.65 ± 35.22	0.03*
Leptin in follicular fluidng/ml	78.32 ± 18.11	93.77 ± 21.01	0.013*

Figure1: percentages of pcoscharacteristics finding among PCOD patient Correlation was done to measure the relationship between BMI, insulin and leptin in serum and in follicular fluid and are illustrated in table 3.

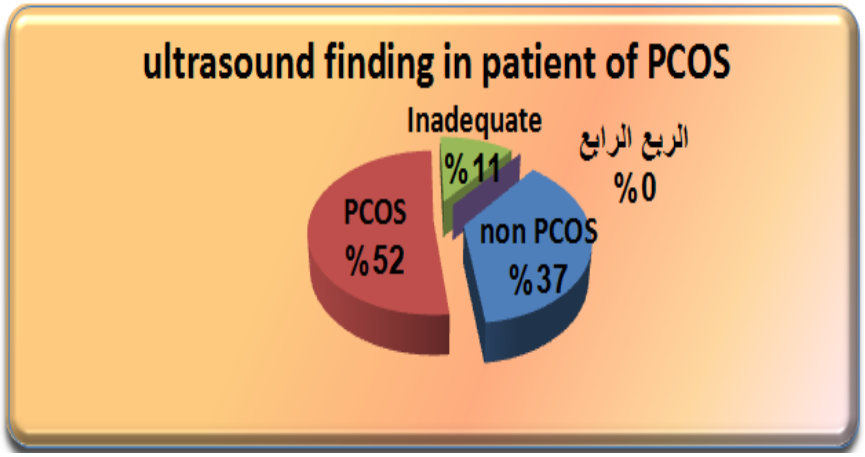

Table3: shows different correlation in pcos patient and control group

Correlation between parameters	Patients	Control
Serum leptin with serum insulin	r=-0.2 p=0.02	r=-0.42 p=0.02
Serum leptin with BMI	r=-0.06 p=0.73	r=-0.02 p=0.91
Insulin in follicular fluid with leptin follicular fluid	r=-0.09 p=0.49	r=-0.2 p=0.43
Leptin in follicular fluid with serum insulin	r=-0.07 p=0.06	r—0.04 p=0.84
Insulin in follicular fluid with serum insulin	r=-0.002 p=0.99	r=0.10 p=0.6
Insulin in follicular fluid with BMI	r=0.2 p=0.33	r=-0.2 p=0.35
Serum insulin with BMI	r=0.02 p=0.91	r=-0.12 p=0.54

IV. Discussion

PCOS, the common dysovulatory infertility, is characterized by chronic anovulation and hyperand rogenemia. These features manifest with advancement of age and gradual increase of adipose tissue, which are often linked to leptin and its receptor(5) .Obesity is common in more than the half of women with PCO. The central fat distribution (android obesity) exacerbates the risks of diabetes mellitus and cardiovascular disease. Although in this study it was found that there is no significant difference between patients and control regarding BMI ,and there is weak correlation between serum leptin and B MIwhich was 30kg/cm$^{2.}$(±5.613). The explanation for our higher incidence of overweight may be attributed to the food habits adopted in Iraq and to the lack of exercise among Iraqi women. In 2015 Royal College of Obstetricians and Gynaecologists showed thatLH may be elevated, with the LH:follicle-stimulating hormone (FSH) ratio increased (>2), with FSH normal; however, this is not part of the diagnostic criteria and may be normal.In this study there was significant difference between patients with PCOS and control group regarding serum LH .While there was no significant difference regarding FSH.Significant difference in serum estrogen between patients and control was found in this study ,though its relation to the level of leptin is poorly understood as Jana Chacarbarti said in his study in 2016(7

Marfan Mohammad and Ashraf Olabi in 2016(8) were found that serum Leptin levels were correlated positively with BMI in Patient and control groups. This result is in agreement with many studies have reported that leptin is correlated to BMI in both groups, in this study there's positive correlation between S. leptin and BMI in patients group while negative correlation between theme in control group.A recent study by Olszanecka Glinianowiczetal(2013)demonstratedhigherleptinlevelsin PCOS subjects compared with control group and this goes with this study in which there is significant difference between patients and control regarding leptin level in serum and follicular fluid(9). Several studies showed that leptiniscor related with insulinlevelin PCOS subjects(10), though other studies demonstrated no correlation like Nasser M.Rizkand Elham Sharif in 2015(11) who did notillustrate any worthy correlation between insulin and leptin in their study. this study demonstrate negative correlation between insulin and leptin in follicular fluid in the control group, while positive correlation between them in patients group.The controversy could beat tributed to the differenc esinthesamplesize ,the study populations, and the heterogenicnature of the PCOS syndrome.

III. Conclusion

From this study we can conclude that significant inverse relation was found between serum insulin and serum leptin in both patient and control group. non significant difference was found in FSH, BMI between thetwo groups.

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