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EVALUATION OF ADIPONECTIN HORMONE IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is common complex endocrine disorder affects5-10% of women during reproductive age 30%-75% of cases of pcos associated with central obesity is often due to increased visceral fat unified metabolic dysfunction of the syndrome. Adiponectin is a cytokine produced and secreted exclusively from adipose tissue but the relationship between Adiponectin & PCOS remains controversial. The objective of this study is to evaluation Adiponectin and luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T) concentration in women with PCOS Ninty infertile obese women {obesity class BMI1-11} within age range {15-35years} subdivided according to Rotterdam criteria to 69 women with PCOS and 21 non PCOS. They were prospectively recruited for this study from Infertility diagnosis outpatient clinic centre in south of Iraq myssan during a period from April-2014 to November 2014. All women agreement to be fasted over night for venous blood sample drain at the morning of the 2nd day of cycle to estimate plasma Adiponectin, LH, FSH and T. Measurements of weight in kg, height in meter waist circumference in cm, hip circumference in cm, was done for calculation of body mass index (BMI) kg/m^2 & W/h. The mean serum value of ADP in non PCOS was higher than of PCOS (17,8ng/ml± 6.38 vs 4.2ng/ml±2.53) with a significant association (P value =0.0001), In conclusion Hypoadiponectinemia is evident in obese infertile women with PCOS as well proportional indirectly with W and W/H which is indicator of visceral obesity & associated of metabolic risk Hypoadiponectinemia was highly significant correlation with primary infertility which is associated abnormalities of PCOS.

KEYWORDS: PCOS, ADP, ELISA, LH, FSH, T, W. W/h, BMI.

INTRODUCTION

PCOS known as Stein-Leventhal syndrome were firstly described by Stein and Leventhal.[1] since 1935 in 20 century up to day PCOS became wild world well knowingly by author as one of the most common complex, endocrine metabolic disorders of humans and particular endocrine abnormality of women at reproductive age. 18% of PCOS women has been diagnosed based on Rotterdam diagnostic criteria.[2] which involved wide range of PCOS representatives as heterogeneous disease characterized by an ovulation, hyper androgenaemia or polycystic ovaries, Infertility in 75% of PCO's women[3], due to high number of arrested small antral follicles that's lead to an ovulatory cycles which reflects menstrual irregularities either Oligomenorrheaor Amenorrhea the last is the usual presented complain in gyn-clinic with or no associated signs of androgen excess[4] including acne hirsutism, alopecia, obesity Alopecia and hirsutism signs of high androgen in pcos women[5] but show variations between women have same values of serum androgen and racial factor play role in its distribution in pcos women also few cases reported females with normal T level but express hirsute[6] high androgen allied to An android fat distribution is observed in hyper androgen females with (PCOS). 40% of women with pcos have been obese and 80% central obesity according to BMI classification while visceral obesity in normal weight.[7] Abdominal obesity appear as protrude lower abdomen extended down word. Authors found PCOS patients to have a five to eight-fold increased risk for type-2 diabetes compared with healthy weight-matched females, thus making the syndrome of high socioeconomic importance).[8] It is evidence from both high androsterone, testosterone androgen levels and the fundamental Insulin resistance (IR). thus hypertension, dyslipidemia and hyper insulinemia are highly reliant on obesity, which worsens the clinical presentation of PCOS. Abdominal obesity is associated with changed secretion of several adipocyte-derived peptide hormones adipose surrounding sex organs can secrete sex hormones, another adipose tissue hormones, most abundant adipocytokines specially Adiponectin is a fat cell product, mainly secreted from visceral and bone marrow fat cells[9] secreted into the circulating blood, it might be dependable for the metabolic and neuroendocrine derangements. Studies showed that adiponectin gene mutations were associated with increased type-2 diabetes risk in Japanese subjects.[10] The product of this gene is called Adiponectin, amino acid protein with high structural homology to collagen VIII, X complement (C1q) & Tumar Necroting Factor (TNF).[11] Adiponectin expression is increased by peroxisome proliferators-activated receptor agonists subsequent characteristic of

obesity and obesity-related disease, such as PCOS. low levels of Adiponectin have been more closely correlated to the degree of IR than adiposity mass.[12] The starting troubles associated with the pcos are the bidirectional disorder of thymulin in the reproductive-endocrine function of the hypothalamic–pituitary– Gonadal (HPG) axis due to insulin resistance and high insulin level subsequent disturbances in secretion of LH and FSH level and rhythm,[13] Adiponectin has a role in the anticipation anti atherogenisis antidiabetes, inflammatory, insulin sensitizing effects and is negatively linked to the extent of adipose tissue in well persons.[14] Studies showed that high adiponectin levels may protect against insulin resistance and type-2 diabetes Although the physiological role of Adiponectin in PCOS still has to be clarified.[15]

OBJECTIVE

Evaluation (ADP) concentration in women with (PCOS) and luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T) study may reflects possible correlations of adiponectin to PCOS and other associated symptoms such as infertility, obesity parameters (W/H ,W).

Design

across-sectional study with descriptive analytic elements. Place: Infertility diagnosis outpatient clinic medical centre in south of Iraq myssan during a period from April -2014 to November-2014.

Patients & data collection

Patient (s): participating 90 obese women infertile for (1-15) years duration, Obese (obesity class BMI 1-11) within age range (15-35years) were subdivided to tow group first sample group diagnosed with PCOS 69 infertile obese women fulfilling at least two of the following three criteria based on Rotterdam criteria.[16] Oligomenorrhea or amenorrhea clinical or biochemical hyperandrogenism. Ultrasonography polycystic ovarian morphology. and the rest 21 non PCOS control group infertile free of signs and symptoms of PCOS. All women, agreement to participate in the study to be fasting over night (10-12-hour) and presented at the morning of 2nd day of her menstrual cycle, Fasting blood samples were drawn in the follicular phase (cycle days 2–3) in all controls and in patients with a cycle length shorter than 3 months; for patients with cycle length longer than 3 months, induction of menstrual cycle by 50mg progesterone injection Intra muscularly.

Exclusion criteria

Diabetic patients, hypertension, Chronic renal disease, proteinuria, Smoking, alcohol use, Medication usage, late-onset congenital adrenal hyperplasia, hyper- prolactinaemia, history of recent administration of hormonal therapy at least 6 month including contraceptives, drug apart from metformin, patients with Cushing syndrome, thyroid disorders and other endocrine disease.

Medical History and Physical Examination

General examination body shape. central obesity, blood Pressure by using mercury sphygmomanometer medical chest stethoscope examination, gynecological examination and Transvaginal Ultrasono- graphy (TVU) scanner was done by using a high frequency probes (>60 MHz) for recognized polycystic ovary. Ultrasound examination was done on day12 of menstrual cycle to detect the number of follicles >25 with pearl string sign and their size < 12 mm Ovarian volume is measured by the ellipsoid formula which is (length x height x width x0.523)=>10 mm^3.).[17]

Anthropometric measurement

The anthropometric measurements used to the following measurements: 1-Weight in kilograms, 2-Waist in cm, 3-Height in meters 4-calculated Body mass index (BMI): BMI =Weight (kilograms)/Height (meters2) 5- waist hip ratio calculated by dividing the waist measurement by hip measurement.

Female Hormonal Assays: Blood sampling

In the 2^{nd} day of cycle after fasting overnight 10-12 hours fasting blood glucose level measured lower than (p-glucose) < 6.0 m mol/l), fasting Venous blood sample (5 ml) was collected from each women by vein puncture at morning between 8:00A.m to 9:00 A.m, the serum obtained by putting the blood samples in a clean dry plain plastic tube and allowed to clot at 37^oC for 30 minutes before centrifugation. The tubes were centrifuged at 2500 rpm for 5 minutes samples were stored in deep frozen at- 20°C until hormonal assays was perform. Hormonal analysis For FSH, LH, T, in serum was determined by an automated mini VIDAS system (Bio MERIEUX SA France Company). FSH, The kits were purchased from Bio Merieux and labeled VIDAS®. Serum Adiponectin determined by using ultra sensitive ELISA Human Adiponectin (ADP) ELISA Kit Cusabio Biotech .co limited, China.) The data was linear by plotting optical density logs against the log of ADP concentrations Calculation of result using the skilled soft "Curve Expert1-3"to create typical curve. This procedure will

produce an adequate with minimum error of the data.

statistical analysis Data were summarized using Statistical packages for social science, version 16.0 (SPSS-16.0). Data were obtainable in form of table of number, percentage and variables were expressed as mean+ standard error (SE), while nominal variables were expressed as number and percentage. Pearson's correlation coefficient was used to evaluate correlation between numeric variables. Chi-square test (χ2-test) and self-determining sample T-test was used for testing the significance of association between variable under study. Statistical significant was considered when the P-value was equal or less than 0.05.

RESULT

In this study 90 obese and infertile woman; total sample studied included 69(76.9%) were diagnosed PCOS and 21(23.1%) were had non-PCOS. The tow sample matched for Age and BMI and there was no significant association between both group in this study as showing in table 1. Where the Mean age ±SD was (26.2 8± 5.25), for PCOS, for non-PCOS was (28.19 ±3.85) no significant association (P value = 0.121). At the same table Mean BMI ±SD (PCOS = (36.4 ± 2.7) & (non PCOS= (36.5 ±2.4) no significant association (P value =0.39).

Table {1}: Mean and Stander Error SE for Age & BMI of both group.

	Mean ± SD PCOS69	SE	Mean ± SD non PCOS 21	S E	P value
Age(year)	26.28±5.25	.62	28.19±3.85	.84	0.121
BMI kg/m^2	36.4±2.7	0.32	36.5±2.4	0.52	0.39

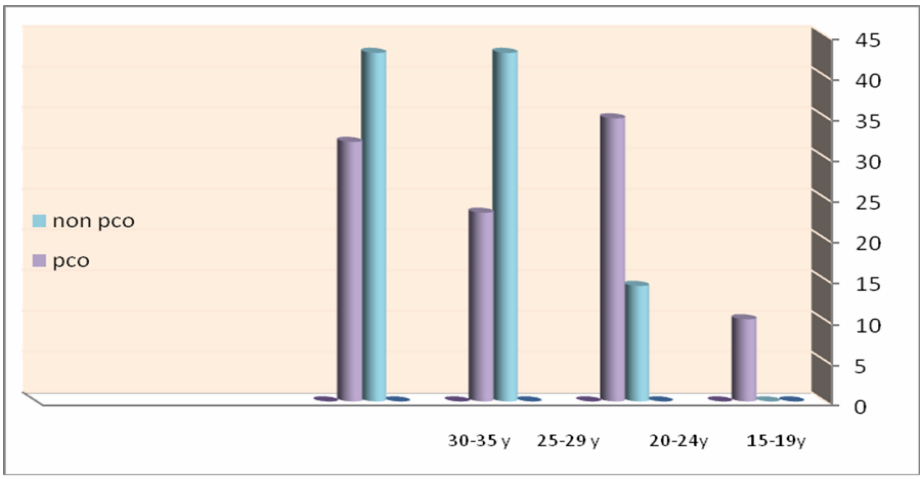

Figure {1}: Distribution of study sample according to age group.

Table 2 shows that the mean serum value of ADP in non PCOS was higher than of PCOS

(17,8ng/ml± 6.38 vs 4.2ng/ml±2.53) with a significant association (P value =0.0001), ADP& Obesity class ADP serum level had difference in its mean in obesity class I and II (9.41ng/ml ±8.27 Vs 6.38ng/ml±6.08) and significant association was found (p value0.05).

Table 2 mean serum value of ADP in infertility and obesity class in infertile obese women with PCOSand without.

table 2		No.	ADP Mean ± SD	SE	P value
Women	PCOS	69	4.2± 2.53	.303	0.0001*
	Non PCOS	21	17.8 ± 6.38	1.39	
BMI kg/m^2	class I	27	9.41 ± 8.27	1.59	0.05*
	class II	63	6.38 ± 6.08	0.76	
infertility	Primary	55	5.97 ± 5.06	0.68	0.001*
	Secondary	35	9.81 ± 8.61	1.45	

ADP & infertility type the study show the mean of serum level of ADP in primary infertility was (5.97ng/ml±5.06) and in secondary infertility was (9.81ng/ml ±8.61) with a significant association between adiponectin hormone & types infertility (p value 0.001).

ADP hormones and other variable in this study found the correlation between serum ADP and some variable (infertility, obesity, duration) and other hormones (LH, FSH, Testosterone and Ratio of LH/FSH) in which only significant correlation was present between Adiponectin and infertility (P value = 0.009) and between Adiponectin and Testosterone hormone (p value=0.001) as showing in table. 3.

Table. 3 Correlation of adiponectin with hormone & other variable.

table 3 ADP H.		r	P value
Hormones	LH(IU/L)	-.080	.454
	FSH(IU/L)	.175	.101
	Test(ng/ml)	.366	.001*
	LH / FSH	-.396	.068
Infertility duration		0.100	0.364
Infertility type		0.274	0.009*
BMI(kg/m^2)		0.186	0.080
Age (year)		0.143	0.179

Table 4 shoes that there was a significant difference in LH level in both PCOS (6.08 IU/L± 3.76) and non PCOS (3.48±3.06) with significant association (p value 0.011) while there was no difference for FSH between PCOS (6.09 IU/L ± 7.16) & non PCOS (6.42 IU/L±5.96) (P value = 0.846), LH /FSH again a relative difference in LH/FSH in both PCOS (1.14± .58) and non PCOS (0.55 ±.26) with significant statistical association (P value = 0.003), Testosterone

studied sample PCOS (1.11ng/ml ±1.021) to non PCOS (0.82ng/ml ±0.59). Although there was no significant statistical association (p value 0.70).

Table 4 Hormones and other variables in patients and control.

table 4		Non PCOS 21		PCOS 69		P value
		Mean ± SD	SE	Mean± SD	SE	
ADP H ng/ml		17.8±6.38	1.39	4.2 ± 2.53	.303	0.0001*
LH IU/L		3.48±3.06	6.66	6.08± 3.76	.44	0.011*
FSH IU/L		6.42± 3.96	1.30	6.09 ± 7.16	.86	0.84
LH / FSH		0.55 ± .26	.107	0.94 ± .58	.145	0.003*
Testosterone ng/ml		0.82±0.59	0.13	1.11±1.021	.122	0.07
BMI kg/m^2		36.5 ± 2.4	0.52	36.4 ± 2.7	0.32	0.39
Infertile duration		5.33±3.21	0.7	5.88± 3.81	0.47	0.56
W/ H		0.81 ±0.04	0.11	0.89±0.05	0.005	0.08
obesity	class I	28. 6%		30.4%		0.9
	class II	71.4%		69.6%		
Infertility	Primary	33%		69.6%		0 .003
	2ndary	77%		31.9%		

DISCUSSION

Women in this study sample and control had a comparable mean Age and BMI to eliminate any variations that may affect the results of the measured biochemical parameters.

Primary infertility in women with PCOS was higher 48/69 than in those with non PCOS 7/14 (69.6%, 33.3% respectively) there was a significant statistical association present between primary infertility and PCOS (P value=0.003) and ADP hormone mean serum level show lower (Hypoadiponectinemia) in PCOS group (p value=0.0001) and in primary infertility (p value=0.009) this point is of value because PCOS is the main cause of infertility in this study specially young age< 24 years which mean that there is risk of metabolic disturbance making difficulties in treatment of PCOs[18] and that's keep it up for several years; The question is what happen if we increase the ADP serum level in blood before or with treatment of pcos. Form other view Hypoadiponectinemia in increased BMI in PCOS group again are predictive metabolic risk for such reason being primary type of infertility prevalence < 24 years and 2ndry infertility in older than 25 years there is significant association in pcos and age (P value = 0.045). While ADP not. with peak of infertility of both type over 30 years in Iraqi obese women because CO plus PCOS the main factors affected women fecundity in this study and this fact found by (Batista, et al) that women age over 34 years old decline of fertility.

In this study, BMI and WHR were the only available measures of body composition. W/h in obese infertile women with similar BMI the high w/h in PCOS above the normal value which is dependent determinants of central obesity making attention of associated central obesity in PCOS which is again risky.[22,23] PCOs (0.89±0.05 & in non PCOS 0.81±0.04} without significant association (P value=0.08).

Hormonal related to ADP in this study T in PCOS patients had A significant correlation between adiponectin and T-testosterone could be caused by insulin resistance as well as high LH/FSH leve). However, our data are supported by previous studies finding significant positive associations between adiponectin and testosterone levels in PCOS.[24] Vribkova et al. suggested that this association was caused by a more complex interrelation between testosterone, oestradiol and adiponectin in PCOS.

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