

Study of Omentin1 and Other Adipokines and Hormones in PCOS Patients

Atheer Mahde, Mahmud Shaker, Zohair Al-Mashhadani

Abstract

Objectives: Polycystic ovary syndrome (PCOS) is associated with insulin resistance and obesity. Recent studies have shown that plasma omentin-1 levels decrease with obesity. Currently, no data exists on the relative correlation between omentin-1 with other adipokines or the expression and regulation of omentin-1 in the serum of women with PCOS. The objective of this study is to evaluate the role of omentin-1 levels or omentin-1 /adipokines ratio in the serum of women with PCOS compared with matched control subjects.

Methods: The study involved 60 patients with PCOS and 30 women without PCOS who were used as controls. To examine the relationship between fasting serum omentin-1 and serum interleukin-6 (IL-6), interleukin-8 (IL-8), resistin, ghrelin, leptin RBP-4 and tumor necrosis factor- α (TNF- α) levels in infertile PCOS and non-PCOS subjects. Also, insulin and other hormones were measured in both groups. All these factors were measured by enzyme-linked immunosorbent assays.

Results: From the total of 60 cases, there was a significant increase ($p < 0.001$) in PCOS patients when compared to the control group in fasting serum, serum interleukin-6 (IL-6), interleukin-8 (IL-8), resistin, leptin RBP-4, tumor necrosis factor- α (TNF- α) levels and insulin. A significant decrease in omentin-1 and ghrelin ($p < 0.001$) was observed. The results also showed that 93.33% and 98.30% in PCOS patients had abnormal

omentin1:Insulin ratio and omentin1:Resistin ratio respectively according to the cut off values ≤ 27.42 and ≤ 31.35 . Moreover, 81.67 % of PCOS patients had abnormal omentin1:IL-6 ratio according to the cut of value (≤ 66.09).

Conclusion: This is the first time the role of plasma omentin1 has been investigated with respect to its implication in PCOS. Usually, LH/FSH ratio and FAI (ratio of total testosterone to SHBG) are the important factors used for the diagnosis of PCOS in all previous literature, but none of them referred to the parameters discussed in this report. Also, the percentage of sensitivity and the difference between range of these parameters in PCOS patients and the controls may give a different perspective in trying to understand the etiology of PCOS. Therefore, these parameters may be used for future diagnosis of PCOS. This study also suggested that omentin/resistin ratio may play a crucial paracrine or endocrine role in modulating insulin sensitivity.

From the Department of Acceptable Analysis, Health and Medical Technical College, Baghdad, Iraq.

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*Address correspondence and reprint request to: Dr Atheer Mehdi, Department of Acceptable Analysis, Health and Medical Technical College, Baghdad, Iraq.
E-mail: atheerawod@yahoo.com*

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Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine metabolic disease that occurs in 5-10% of women of reproductive age.¹⁻³ PCOS is an inherited disease that affects women of childbearing age.⁴

The metabolic syndrome is associated with excessive accumulation of central body fat. As well as its role in energy storage, adipose tissue produces several hormones and cytokines termed adipokines that have widespread effects on carbohydrate and lipid metabolism. They appear to play an important role in the pathogenesis of insulin resistance (IR), diabetes, and atherosclerosis.⁵ Adipose tissue is now hypothesized to be the largest endocrine organ in the body, secreting a large number of biologically important substances termed adipokines. The best characterized adipokines are adiponectin, leptin, TNF- α , and IL-6.⁶ Other identified adipokines include Plasminogen activator inhibitor-1 (PAI-1), resistin, visfatin and glucocorticoids.⁶

These adipokines are postulated as a potential link between abdominal obesity and the vasculature, and have been shown to mediate IR.⁷ Numerous studies have also found associations between IR and increased TNF- α , IL-6, macrophages and monocyte chemoattractant protein-1 (MCP-1), in addition to PAI-1, adipin, and decreased adiponectin.⁸

Omentin1 (also named Omentin, Intelectin-1, Endothelial Lectin HL-1 and Intestinal Lactoferrin Receptor) has been identified as a major visceral (omental) fat secretory adipokine.⁹ The mature omentin is a secretory glycoprotein consisting of 295 amino acids and N-linked oligosaccharides, and its basic structural unit is a 120-kDa homotrimer in which 40-kDa polypeptides are bridged by disulfide bonds. It is secreted by omental adipose tissue, much less in the intestines, lung and heart and highly abundant in human plasma.⁹

Omentin-1 is a new type of Ca^{2+} -dependent lectin with affinity for galacto furanosyl residues (constituents of pathogens and dominant immunogens).¹⁰ It was suggested, therefore, that a biological function of omentin/intelectin was the specific recognition of pathogens and bacterial components, an important role in the innate immune response to parasitic infections.¹¹ Moreover, several studies have shown that omentin gene expression is altered by inflammatory states and obesity.¹²

Kuperman *et al* (2005) found increased gene expression of omentin in airway epithelial cells of patients with asthma.¹³ Intriguingly, differential expression of omentin mRNA occurs in omental adipose tissue of patients with Crohn's disease, suggesting that omentin could be a new candidate factor potentially involved in chronic inflammatory diseases in humans.¹⁰

A homolog of omentin has been identified that it shares 83% amino acid identity with omentin/intelectin and it may be referred to as omentin-2.¹⁴ The two omentin genes, omentin-1 and omentin-2, are localized adjacent to each other in the 1q22-q23 chromosomal region, which has been previously linked to Type II Diabetes Mellitus in several populations.^{15,16-19}

In vitro studies have shown that omentin increases insulin signal transduction by activating the protein kinase Akt/protein kinase B and enhancing insulin-stimulated glucose transport in isolated human adipocytes.⁹

Lean subjects had significantly higher plasma omentin levels than obese and overweight subjects. In addition, higher plasma omentin levels were detected in women compared with men.²⁰

Omentin-1 is decreased in patients with PCOS, a disease associated with IR and obesity.²¹ Glucose and insulin negatively regulate Omentin1 levels *ex vivo* and *in vivo*.²¹ Therefore, omentin levels may be predictive of the metabolic consequences or comorbidities associated with obesity.

Methods

Subjects

Samples

After fasting overnight, the venous blood samples were aspirated at 08:00-10:00 am during the 3rd-6th day of the menstrual cycle (early follicular phase) for patients with normal cycles. For patients with ovulation or oligomenorrhea, blood samples were collected regardless of the duration of the cycle. The samples were transferred into clean, plain tubes and centrifuged within 30 minutes of collection. Then the serum from all blood samples were separated; sugar and lipid profile levels were measured using enzyme colorimetric methods and the rest were stored at 18°C until the time of assay.

Patients

60 infertile Iraqi women aged 18-37 years ($M \pm SD$: 26.45 ± 4.65) were enrolled for the study. Their medical histories were noted, body weight and height were measured, and body mass index (BMI) was calculated [mean BMI ($34.01 \pm 3.54 \text{ Kg/m}^2$)]. PCOS patients had already been diagnosed and the diagnosis was confirmed according to the European society of human reproduction and embryology and American society for reproductive medicine criteria; PCOS is diagnosed if there are any two of the following:

- Presence of polycystic ovary on ultrasound examination.
- Clinical or biochemical hyperandrogenemia.
- Menstrual dysfunction with an ovulation.

Healthy Control Group

For comparison, thirty apparently healthy fertile women with regular cycles who matched for age, weight, and BMI [$n=30$; age= 28.87 ± 3.27 (years); BMI= 29.56 ± 2.12 (kg/m^2); mean \pm SD] were also included as control subjects.

Protocol

Clinical and anthropometrical variables, including clinical blood pressure, BMI, (calculated as kg/m^2) and waist-to-hip ratio (WHR) were determined in all the subjects. Omentin-1, IL6, IL-18, resistin, TNF- α , ghrelin, RBP-4 leptin, insulin, LH, FSH, total testosterone, free testosterone and sex hormone-binding globulin (SHBG) were determined by ELISA methods. Serum fasting glucose level was measured by enzymatic method supplied by Giese Diagnostics.

The homeostasis model assessment (HOMA) was used to calculate an index of insulin resistance for each patient, and beta-cell function was estimated from fasting insulin and glucose levels by the homeostasis model assessment ($\text{HOMA-}\beta$). Using the fasting glucose (mmol/L) and insulin ($\mu\text{IU/ml}$), the index for insulin resistance; HOMA IR , was defined as $(\text{insulin} \times \text{glucose})/22.5$ and $\text{HOMA } \beta\text{-cell function} \times 20 \times \text{insulin}/(\text{glucose}-3.5)$.²²

Statistics

All statistical analysis in the study were performed using SPSS version 15.0 for Windows (Statistical Package for Social Science, Inc., Chicago, IL, USA). Descriptive analysis was used to show the mean and standard deviation of the variables.

The significant difference between mean values was estimated by the Student t-test. The point of statistical significance was noted when probability was $p < 0.05$, and no statistical significance

was noted when $p > 0.05$. Correlation analysis was used to test the linear relationship between parameters. ANOVA test was used to show the differences between variables of differentiated groups.

Result

Compared with normal controls, the results showed that women with PCOS had increased ($p < 0.001$) levels of IL-6, IL-18, TNF- α , RBP-4, Resistin, leptin, insulin, LH, testosterone, free testosterone,

HOMA, and HOMA β -cell% (table 1). Furthermore, patients with PCOS also had lower omentin-1 ($p < 0.001$), ghrelin ($p < 0.05$) and QUICKI ($p < 0.001$) values than controls (table 1), while FSH and FBG levels were not significantly different ($p > 0.05$) between the two groups. The PCOS patients were divided into 2 groups. Group 1; thirty one PCOS patients with irregular menstrual cycles (oligomenorrhea, amenorrhea) and group 2; twenty nine PCOS patients with regular menstrual cycles (table 2).

Table 1: Clinical and baseline Adipokines, hormone concentrations in PCOS and control groups.

Characteristic	PCOS mean \pm SD	Control mean \pm SD	p (t-test)
BMI Kg/m ²	33.14 \pm 1.88	29.56 \pm 1.01	<0.001
WHR	0.86 \pm 0.02	0.80 \pm 0.02	<0.001
TNF- α pg/ml	5.56 \pm 1.53	2.98 \pm 0.51	<0.001
IL-6 pg/ml	5.82 \pm 1.66	2.75 \pm 0.66	<0.001
IL-18 pg/ml	298.98 \pm 107.34	229.60 \pm 55.34	<0.001
RBP-4 μ g/ml	35.11 \pm 6.51	27.33 \pm 3.49	<0.001
Resistin ng/ml	13.78 \pm 2.26	7.66 \pm 0.66	<0.001
Leptin ng/ml	31.92 \pm 2.39	28.08 \pm 1.63	<0.001
Ghrelin pg/ml	138.22 \pm 58.40	169.67 \pm 25.51	<0.05
Omentin-1 ng/ml	252.45 \pm 33.39	327.50 \pm 40.34	<0.001
Insulin μ U/ml	20.93 \pm 8.38	8.05 \pm 0.64	<0.001
FBG mg/dl	86.0 \pm 7.00	85.57 \pm 6.39	>0.05
HOMA	4.61 \pm 2.06	1.58 \pm 0.16	<0.001
HOMA β -cell%	375.90 \pm 194.70	132.86 \pm 33.48	<0.001
QUICKI	0.31 \pm 0.02	0.35 \pm 0.01	<0.001
LH IU/L	14.91 \pm 2.68	9.53 \pm 1.77	<0.001
FSH IU/L	5.20 \pm 0.71	5.54 \pm 0.85	>0.05
Testosterone nmole/L	2.66 \pm 0.40	2.18 \pm 0.27	<0.001
Free testosterone pg/ml	3.87 \pm 1.24	2.12 \pm 0.49	<0.001
SHBG nmole/L	5.25 \pm 3.72 3	53.06 \pm 4.95	<0.001
FAI %	7.98 \pm 0.85	5.19 \pm 1.33	<0.001

PCOS: Polycystic ovary syndrome; BMI: Body mass index; WHR: Waist-to-hip ratio; TNF: Tumor necrosis factor; IL: Interleukin; RBP: Retinol binding protien; FBG: Fasting blood suhar; HOMA: Homeostasis model assessment; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone; SHBG: Sex hormone-binding globulin; FAI: Free androgen index; QUICKI: Quantitative insulin-sensitivty check index

Table 2: Clinical and baseline Adipokines, hormone concentrations in PCOS with irregular and regular menstrual cycle

Characteristic	PCOS (Irregular menstrual cycle) mean \pm SD	PCOS (Regular menstrual cycle) mean \pm SD	p (t-test)
BMI Kg/m ²	33.87 \pm 1.66	32.36 \pm 1.81	<0.001
WHR	0.87 \pm 0.02	0.86 \pm 0.02	>0.05
TNF- α pg/ml	6.47 \pm 1.21	4.58 \pm 1.211	<0.001
IL-6 pg/ml	6.37 \pm 1.68	5.23 \pm 1.54	<0.001
IL-18 pg/ml	361.42 \pm 79.99	232.24 \pm 92.15	<0.001

Table 2: Clinical and baseline Adipokines, hormone concentrations in PCOS with irregular and regular menstrual cycle -continued

Characteristic	PCOS (irregular menstrual cycle) mean ± SD	PCOS (Regular menstrual cycle) mean ± SD	p (t-test)
RBP-4 µg/ml	36.15±6.14	33.86±5.26	>0.05
Resistin ng/ml	14.84±2.22	12.66±1.70	<0.001
Leptin ng/ml	32.83 ± 1.94	30.95 ± 2.47	<0.001
Ghrelin pg/ml	108.39±49.96	160.10±49.72	<0.05
Omentin-1 ng/ml	237.32±23.42	260.24±57.00	<0.001
Insulin µU/ml	25.38 ±7.88	16.17±6.00	<0.001
F.BG mg/dl	87.68±8.11	85.44±5.50	>0.05
HOMA	5.69 ±1.96	3.46±1.47	<0.001
HOMA β-cell%	455.00 ±207.00	291.34±140.13	<0.001
QUICKI	0.30 ±0.01	0.32±0.01	<0.001
LH IU/L	14.68 ±2.34	15.16±3.03	>0.05
FSH IU/L	5.17 ±0.77	5.23±0.66	>0.05
Testosterone nmole/L	2.65 ±0.35	2.64±0.37	>0.05
Free testosterone pg/ml	3.81 ±1.37	3.94±1.10	>0.05
SHBG nmole/L	5.57 ±3.79 3	34.91±3.68	>0.05
FAI %	7.93 ±0.94	8.02±0.76	>0.05

PCOS: Polycystic ovary syndrome; F.BG: Fasting blood suhar; HOMA: Homeostasis model assessment; QUICKI: Quantitative insulin-sensitivty check index; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone; SHBG: Sex hormone-binding globulin; FAI: Free androgen index

There was a negative correlation in Omentin-1[ng/ml] with BMI (r=-0.435, p<0.001), insulin (r=-0.424, p<0.001), HOMA (r=-0.415, p<0.001), HOMA β-cell% (r=-0.358, p<0.001), LDL-cholesterol (r=-0.328, p<0.05), IL18 (r=-0.411, p<0.001), IL6 (r=-0.458, p<0.001), TNF-α (r=-0.431, p<0.001), RBP4 (r=-0.378, p<0.05), resistin (r=-0.428, p<0.001), and leptin (r=-0.370, p<0.01) between the PCOS group and the control group. A significant positive correlation was found between omentin1 (ng/ml), and QUICKI ([r=0.497, and p<0.001), ghrelin (r= 0.511, p<0.001) as shown in table 3.

Table 4 shows a number of parameters which depend on cut-off values (values above or below the mean ± 2SD) and according

figure 1, 2 respectively. Table 5 figure 1 and 2 show the cut-off values (values ± 2 SD of the mean) from which sensitivity was calculated.

In this study, a significantly negative association between omentin-1/resistin and insulin ratio was found in PCOS patients while there was no significant correlation between insulin and omentin in the control group (figure 3).

Table 3: Baseline Pearson correlations coefficients of omentin1 levels with various metabolic and hormonal parameters in patients with PCOS.

Variable	Omentin1	
	Correlation	p value
BMI (Kg/m ²)	-0.435	<0.001
Fasting insulin (µU/ml)	-0.424	<0.001
HOMA	-0.415	<0.001
HOMA β-cell%	-0.358	<0.05
QUICKI	-0.497	<0.001
Ghrelin (pg/ml)	-0.511	<0.001
IL18 (pg/ml)	-0.411	<0.001
IL6 (pg/ml)	-0.458	<0.001
TNF-α (pg/ml)	-0.431	<0.001
RBP4 (µg/ml)	-0.378	<0.05
Resistin (ng/ml)	-0.428	<0.001
Leptin (ng/ml)	-0.370	<0.01

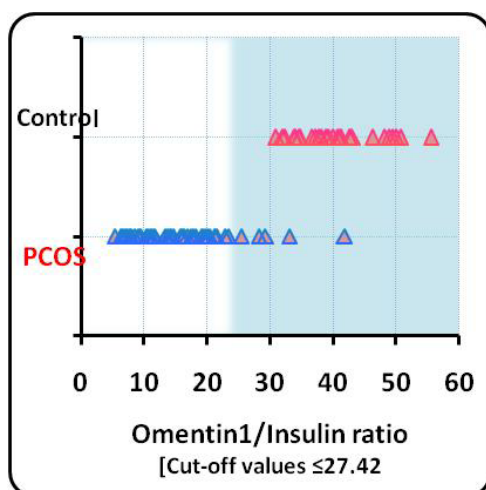
BMI: Body mass index; HOMA: Homeostasis model assessment; IL: Interleukin; TNF: Tumor necrosis factor; QUICKI: Quantitative insulin-sensitivty check index; RBP: Retinol binding protien

Table 4: Omentin1 ratios in PCOS patients compared to control.

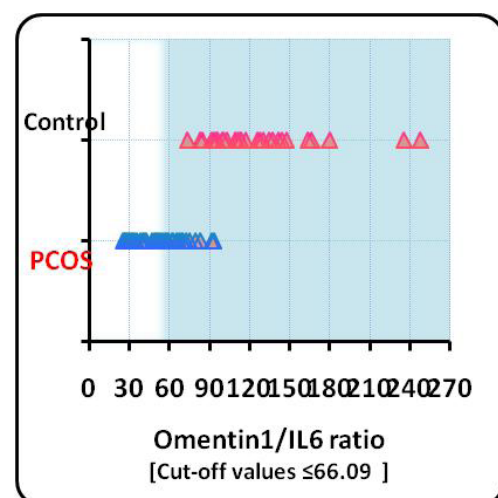
Characteristic	PCOS [n=60 [Mean± SD	[Control [n=30 Mean± SD	P
omentin1 : Insulin ratio	14.57±7.44	40.98±6.78	<0.0001
omentin1 : IL18 ratio	1.02±0.54	1.52±0.30	<0.0001
omentin1: IL6 ratio	48.11±18.33	126.99±30.4	<0.001
omentin1 : TNF-α ratio	50.78±22.59	112.41±22.32	<0.0001
oitar 4PBR: 1nitnemo	7.53±2.08	13.17±2.25	<0.0001
oitar nitsiseR: 1nitnemo	19.05±5.26	42.89±5.77	<0.0001
oitar nitpeL: 1nitnemo	7.99±1.55	11.26±1.18	<0.0001
oitar AMOH: 1nitnemo	68.91±38.01	209.25±38.11	<0.0001
oitar %llec-β AMOH : 1nitnemo	0.87±0.50	2.61±0.70	<0.0001

Table 5: The sensitivity of omentin1 ratios in PCOS.

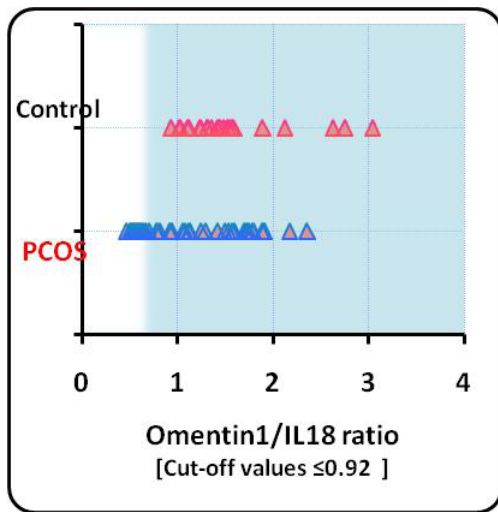
Test	Sensitivity
omentin1 : Insulin ratio ≤27.42	93.33%
omentin1 : IL18 ratio ≤0.92	55.00 %
omentin1 : IL6 ratio ≤ 66.09	81.67 %
omentin1 : TNF-α ratio ≤67.77	81.67%
omentin1 :RBP4 ratio ≤8.67	71.67 %
omentin1 :Resistin ratio ≤31.35	98.30 %
omentin1 :Leptin ratio ≤8.90	53.00 %
omentin1 :HOMA ratio ≤133.03	95.00 %
omentin1: HOMA β-cell% ratio ≤1.21	86.67 %



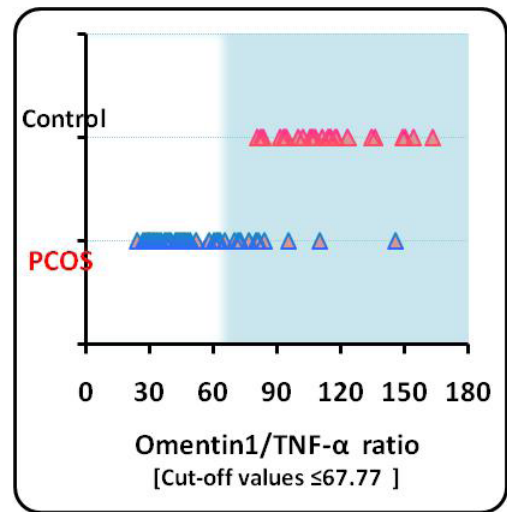
A



B

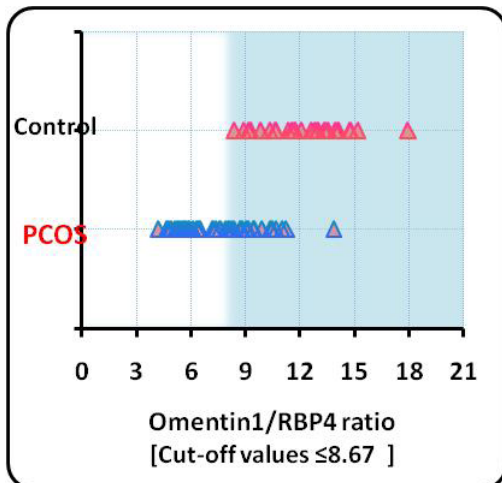


C

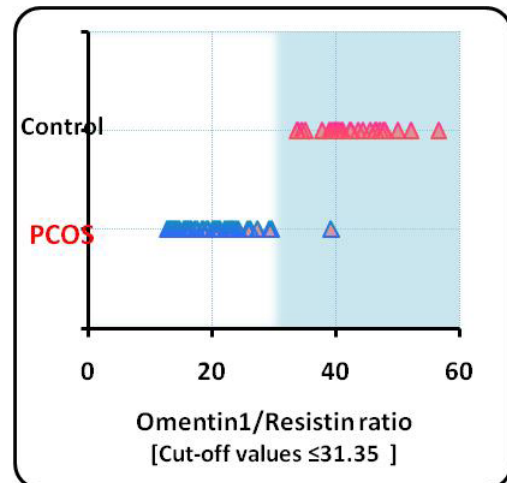


D

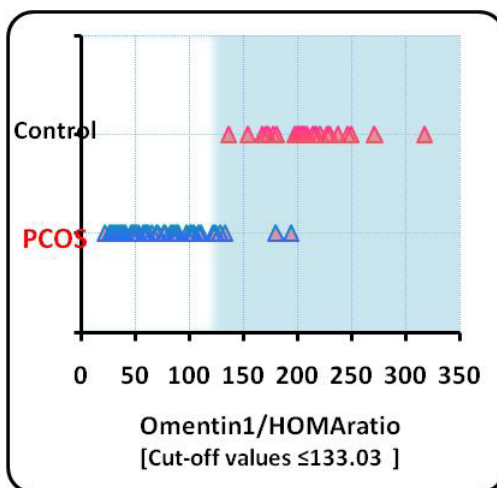
Figure 1: Values for Omentin1/Insulin ratio, Omentin1/IL6 ratio, Omentin1/IL18 ratio and Omentin1/TNF- α ratio (from A to D)



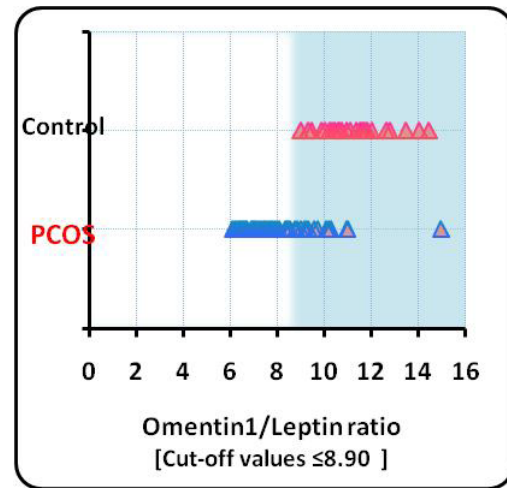
A



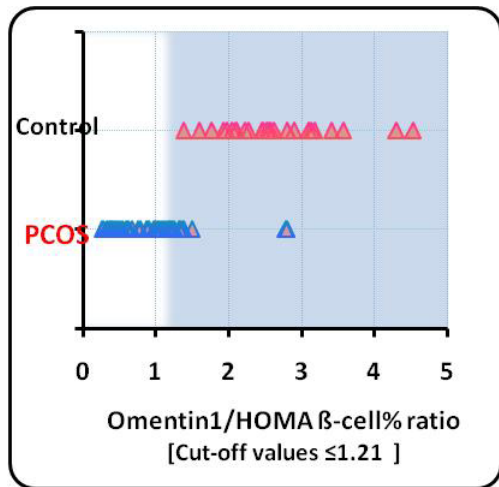
B



C



D



E

Figure 2: Values for Omentin1/RBP4 ratio, Omentin1/Resistin ratio, Omentin1/Leptin ratio, Omentin1/HOMA ratio and Omentin1/HOMA β-cell (from A-E)

In this study, a significantly negative association was observed between omentin-1/resistin ratio and insulin in the PCOS patients while there was no significant correlation was observe in the control group.

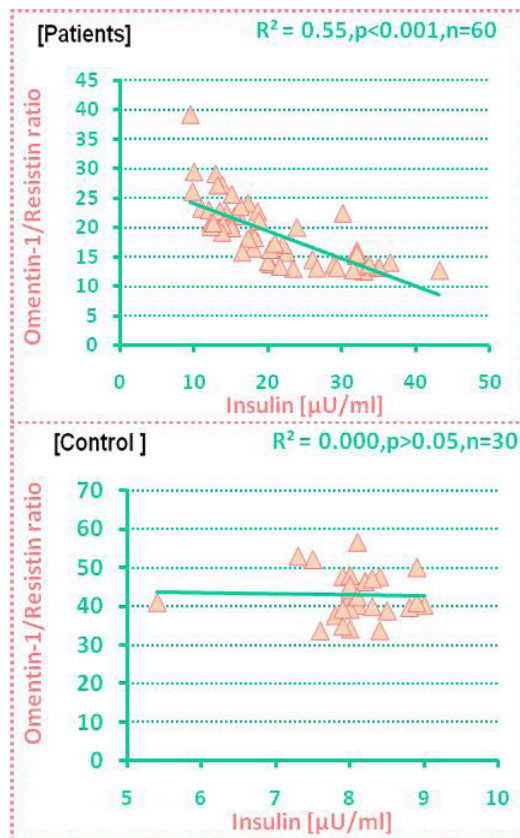


Figure 3. Correlation between omentin/resistin ratio and insulin in PCOS patients and in control.

In this study, a significantly inverse association between omentin-1 /IL-6 ratio and insulin was found in PCOS patients while there was no significant correlation between them in control as shown figure 4.

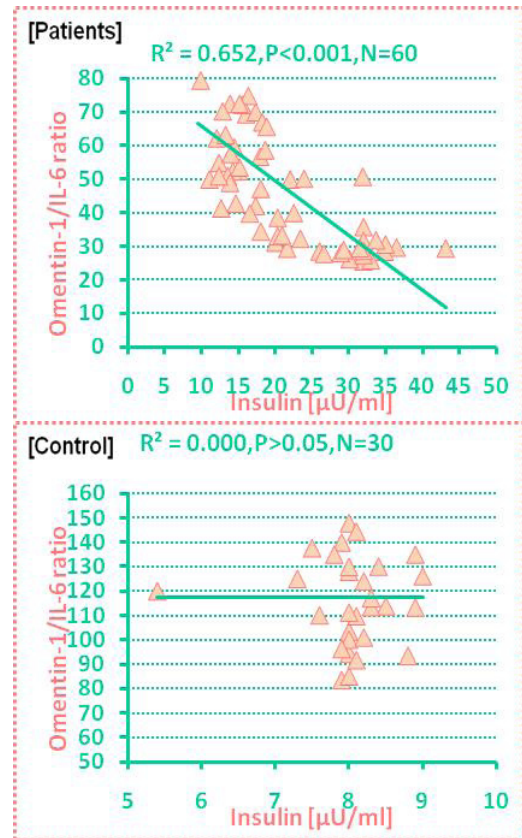


Figure 4. Correlation between omentin-1/IL-6 and insulin in PCOS patients and in control.

Discussion

Obesity is one of the clinical characteristics of the PCOS along with oligomenorrhea, hirsutism, and infertility. However, not all obese females have PCOS and not all PCOS patients are obese. This study also showed a significant increase ($p < 0.001$) in BMI and WHR in PCOS patients (table 1). The cause of obesity in the PCOS patients remains unknown, however, it is thought that obesity may play a pathogenetic role in the development of the syndrome in susceptible individuals.^{23,24} The study showed that women with PCOS in Iraq have a higher body weight than their counterparts.²⁵⁻²⁷ This maybe as a result of different nutritional habits in Iraq than other countries.

26.67% of PCOS patients had normal TNF- α values (≥ 4.00 Pg/ml). Serum levels of TNF- α had been found to be elevated in patients with PCOS compared with age- and/or BMI in the

controlled group, these findings are also consistent with several other studies.²⁸⁻³¹

There was a significant difference ($p < 0.001$) in IL-6 between regular menstrual cycle and irregular menstrual cycle in PCOS patients (table 2). This finding is suggestive of a physiologic modulation of cytokine secretion by the pituitary hormones, although in this study protocol, the gonadotropin stimulation was not observed at any pharmacological dosage. Indeed, previous studies have demonstrated that FSH was able to induce IL-6 expression from granulosa cells, and a possible regulation of IL-6 expression by LH has also been suggested.^{32,33} The increase levels of IL-6 could be in relation to the angiogenesis occurring during the ovarian follicular development.³⁴ In PCOS patients, the intra follicular IL-6 and TNF- α concentrations were higher than those found in the serum, suggesting a local production of these cytokines. Indeed, even if both cytokines are mainly produced by white blood cells, they can also be produced by granulosa cells.³⁵ The mean level of IL-18 was significantly elevated in the PCOS patients compared to the control group [$p > 0.001$] as shown in table 1, a result which is compatible with other studies, while another study did not find any statistical difference between PCOS and the control group.³⁶⁻³⁸ The increase in IL-18 levels found in the PCOS patients was probably related to the visceral adiposity and insulin resistance, frequently found in PCOS patients.³⁹

Serum RBP-4 was found to be significantly elevated ($p < 0.0001$) in PCOS patients with a mean of 35.11 ± 6.51 $\mu\text{g/ml}$ compared to the control group with a mean of 27.33 ± 3.49 $\mu\text{g/ml}$ as shown in table 1. Elevated serum levels of RBP-4 in PCOS were demonstrated in several studies, but another reported that mean basal levels were decreased in PCOS and in the control group.⁴⁰⁻⁴³ There was no significant difference ($p \geq 0.05$) between the two subgroups of PCOS women according to their menstrual cycle, (table 2), this may be due to the fact that RBP-4 concentrations were not correlated with biochemical or clinical endocrine parameters.⁴⁴

The altered levels of resistin may be the consequence of altered adipose tissue function but also as a result of a difference in fat distribution in women with PCOS, because they tend to have proportionally more visceral adipose tissue.⁴⁵ In fact, it has been suggested that differences in adipose tissue distribution may influence the secretion of the different adipocytokines.⁴⁶

Some studies have found that there was no difference in leptin levels between PCOS and control women.^{47,48} Other studies however, found leptin levels in women with PCOS to be higher than expected for their BMI, suggesting abnormalities in leptin signaling to the reproductive system in PCOS.⁴⁹⁻⁵² A study by Basma suggested that leptin was lower in PCOS patients.⁵³ The

differences in the results may be due to different patient number and BMIs. There was a significant difference ($p < 0.001$) in leptin between regular menstrual cycle and irregular menstrual cycle in PCOS patients, (table 2), This finding may be due to the fact that Leptin, a nutrition-and adiposity-dependent protein with a potential to modulate the gonadotropin axis in several mammals, has been proposed to be a possible link between energy metabolism and ovarian function.⁵⁴ Some studies in the literature have suggested that leptin affects fertility through its central and peripheral effects.⁵⁵ Leptin levels are not constant and may vary with follicular growth and maturation and thus fluctuate throughout the menstrual cycle.⁵⁶ Additionally, nocturnal changes in luteinizing hormone pulse parameters are associated temporarily with the rise of plasma concentrations of leptin at night, and the fluctuations of plasma leptin concentrations are synchronous with those of LH and estradiol.⁵⁷

Data on ghrelin levels in women with PCOS are rather conflicting: both decreased, and elevated concentrations have been reported, while others have found no significant differences between women with the syndrome and normal women.⁵⁸⁻⁶² There was a significant difference ($p < 0.001$) in ghrelin between regular menstrual cycle and irregular menstrual cycle in PCOS patients, (table 2), this may be due to the fact that ghrelin is a hormone that can cause reduced secretion of hormones which regulate ovarian and menstrual functions.⁶³

Visceral obesity is highly associated with risks of type II diabetes, cardiovascular disease, hypertension, and hyperlipidemia.^{5,64,65} Expression of adipose-derived factors such as leptin, TNF- α , RBP4, and resistin are modulated by obesity.⁶⁶⁻⁶⁹ Therefore, this study of circulating omentin levels was undertaken to better understand the regulation and role of omentin1, a new visceral fat depot-specific adipokine, in obesity and insulin resistance in PCOS patients. In Iraq, no previous study has clarified the role of omentin1 in PCOS patients or investigated the relationship between omentin and other parameters.

Serum omentin-1 was found to be significantly decreased ($p < 0.0001$) in PCOS patients with a mean of 252.45 ± 33.39 ng/ml compared to controls with a mean of 327.50 ± 40.04 ng/ml (table 1). Decreased serum levels of omentin-1 in PCOS were demonstrated in one study only. 53.33% of patients with PCOS had abnormal omentin-1 values according to the cut-off value ≤ 247.42 ng/ml.²¹ There was a significant difference ($p < 0.001$) in omentin-1 between regular menstrual cycle and irregular menstrual cycle in PCOS patients (table 2), this may be due to the fact that omentin1 can affect the secretion of hormones that

these hormone. This study suggests that more detailed research regulate ovarian and menstrual function or affect receptors for

should be conducted to evaluate the role of novel peptides in women with PCOS.

There is evidence to suggest that omentin-1 may be involved in some aspect of insulin sensitivity, and there was a negative correlation between omentin-1 plasma levels and measurements of insulin resistance (HOMA), fasting insulin, and HOMA β -cell%, but there was a positive correlation with QUICKI and ghrelin. Moreover, negative correlations between plasma omentin-1 levels and BMI, resistin, IL6, IL18, TNF- α and leptin values were observed. There was a negative association between plasma omentin-1 with these metabolic indices suggesting that higher omentin-1 levels may be seen as a marker for leanness or as a positive factor that opposes the obese state and its pathophysiological consequences. Also the data suggests that some aspects of obesity negatively regulates omentin-1 expression and release it into the circulation. Although the data clearly supports the regulation of omentin by obesity, omentin-1 may also be regulated by inflammation. Other studies have shown that omentin-1 expression is altered in inflammatory states.^{10,13} Obesity itself is associated with low levels of chronic inflammation, which may contribute to the regulation in the role of omentin in human physiology.^{70,71} Consequently, weight loss and different inflammatory states could be modulators of omentin-1 expression and function. In summary, there is evidence to suggest that plasma omentin-1 is inversely related to obesity.

In Iraq, there was no study which showed these correlations and this study suggests that omentin-1 is a good index to confirm IR.

The physiological role of omentin-1 in glucose metabolism, omentin's target tissues, a receptor, or relevant signal transduction pathways are still to be determined.

In this study, several parameters that depend on the omentin-1 ratios, (table 4) were observed. Cut-off values determined the sensitivity. These findings are detected for the first time, while LH/FSH ratio and FAI (ratio of total testosterone to SHBG) are the usually important factors used for diagnosis of PCOS in all literature review but none of them referred to present parameters, the good percentage of sensitivity and also the difference between the range of parameters in PCOS and controls may give a different perspective in order to understand the etiology of PCOS. Therefore, the parameters may be useful in determining the diagnosis of PCOS.

In this study, a significantly negative association between omentin-1 / resistin ratio and insulin was found in PCOS patients while there was no significant correlation between them in the control group (figure 3). In vitro studies have shown that omentin increases insulin signal transduction by activating the protein kinase Akt/protein kinase B and enhancing insulin-stimulated

glucose transport in isolated human adipocytes.¹⁰ This study suggested that omentin-1/resistin ratio may play a paracrine or endocrine role in modulating insulin sensitivity.

In this study, a significantly inverse association between omentin-1/IL6 ratio and insulin was found in PCOS patients while there was no significant correlation between them in the control group (figure 4).

Serum IL-6 concentration was positively correlated with obesity and insulin resistance and IL6 expression in adipose tissue with obesity.^{70,71} This study tentatively hypothesized that the decreased omentin-1/IL-6 ratio levels in the serum of women with PCOS as demonstrated in this study may partly explain the corresponding increased levels of insulin observed in the serum of women with PCOS, possibly as a consequence of the hyperinsulinemic state seen in these women. However, these are hypotheses which need to be further investigated. It is important to bear in mind that the regulation of omentin-1 in adipose tissue is probably multifactorial. Moreover, it would be of interest to know whether or not the effects of insulin on omentin-1 production are also applicable to other tissues given the in vivo results observed in this study. Hence, further studies are needed to elucidate the role of other factors that regulate omentin-1 production.

Conclusion

The findings detected in this study have been recorded for the first time, while LH/FSH ratio and FAI (ratio of total testosterone to SHBG) are usually the important factors used for the diagnosis of PCOS in all literature review but none of them referred to present parameters, the % of sensitivity and also the difference between the range of parameters in PCOS patients and control group may give a different perspective in understanding the etiology of PCOS. Thus these parameters can be used for the diagnosis of PCOS. The study also showed that omentin/resistin ratio may play a paracrine or endocrine role in modulating insulin sensitivity.

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