Iraqi JMS

Published by Al-Nahrain College of Medicine
P-ISSN 1681-6579
E-ISSN 2224-4719
Email: iraqijms@colmed-alnahrain.edu.iq
http://www.colmed-alnahrain.edu.iq
http://www.iraqijms.net
Iraqi JMS 2017; Vol. 15(4)

The Relation of Serum Omentin-1 Level with Insulin Resistance in Patients with Polycystic Ovary Syndrome and its Relation with Metformin Treatment

Jumana M. Kareem[1] *MSc,* **Zainab H. Hashim**[1] *PhD*, **Hala A. Almoayed**[2] *ABOG*

[1]Dept. of Physiology and Medical Physics, [2]Dept. of Gynecology and Obstetrics, College of Medicine, Al-Nahrain University, Baghdad, Iraq

Abstract

Background Polycystic ovary syndrome (PCOS) is still a matter of research looking for the true pathogenesis of this enigmatic syndrome. Although the majority of cases are familial, genetic studies have failed so far to identify the specific genes involved. The presentations of PCOS are heterogeneous and may change throughout the lifespan, starting from adolescence to post-menopausal age, and may have health impaction later in life. Omentin-1 is a fat depot-specific secretory protein produced by visceral stromal vascular cells. Recent studies showed that omentin-1 is correlated inversely with obesity and insulin resistance.

Objective To assess the serum omentin-1 concentration in PCOS women and the effect of metformin on omentin-1 level, to evaluate the role of omentin-1 on insulin resistance and hyperandrogenemia in PCOS women and to look for the correlation of omentin-1 with body mass index (BMI) in PCOS women.

Methods Eighty women involved in this study; 40 women with PCOS diagnosed according to Rotterdam ESHRE/ASRMS 2003 criteria and 40 apparently healthy women considered as the control group. The participants were allocated into six groups: "10 obese women with PCOS (BMI ≥30 kg/m^2, without metformin treatment)". "10 obese women with PCOS (BMI ≥30 kg/m^2, taking metformin)". "10 non-obese women with PCOS (BMI <30 kg/m^2, without metformin treatment)". "10 non-obese women with PCOS (BMI <30 kg/m^2, taking metformin)". "20 obese controls and 20 non-obese controls. Blood samples were taken from them for estimation of fasting blood glucose, insulin and omentin-1 levels. Hirsutism score was also evaluated according to Ferriman–Gallwey score.

Results There was a significant increase in omentin-1 in non-obese PCOS (taking metformin) (3.02±0.71) compared to obese PCOS (taking metformin) (1.59±1.48) (P value = 0.0132) and in PCO non-obese (taking metformin) (3.02±0.71) compared with control non-obese (1.96±1.65) (P value = 0.121). No significant correlation was found between serum omentin-1 level and insulin resistance as well as with hyperandrogenemia in any of the six study groups.

Conclusion Omentin-1 is found to be inversely related to body weight in PCOS women. Serum omentin-1 level has no effect on insulin resistance and hyperandrogenism states.

Keywords Polycystic ovaries PCOS, omentin, hyperandrogenemia, insulin resistance

Citation Kareem JM, Hashim ZH, Almoayed HA. The relation of serum omentin-1 level with insulin resistance in patients with polycystic ovary syndrome and its relation with metformin treatment. Iraqi JMS. 2017; Vol. 15(4): 327-338. doi: 10.22578/IJMS.15.4.2

List of abbreviations: ACTH = Adrenocorticotropic hormone, BMI = Body mass index, IGF = Insulin like growth factor, IR = Insulin resistance, LH = Luteinizing hormone, Mgpd = Mitochondrial glycerophosphate dehydrogenase, PCOS = Polycystic ovary syndrome

Introduction

Polycystic ovary syndrome (PCOS) is the most common hormonal defect in child bearing women affecting about 7% of this population. The reproductive manifestation of PCOS consists of excess in androgen production and disordered gonadotropin secretion leading to menstrual irregularity, hirsutism and infertility [(1)]. In addition to these manifestations, PCOS has metabolic characteristics that include prominent defects in insulin action and β-cell function, defects that confer a substantially increased risk for glucose intolerance and type2 diabetes [(2)]. Obesity is a common finding in women with PCOS and between 40-80% of

women with this condition are reported to be overweight or obese [3].

Insulin resistance (IR) is the most conjoint finding in PCOS that is independent of obesity. Insulin-mediated glucose dumping, reflecting mainly insulin action on skeletal muscle is decreased by 35-40% in women with PCOS related to weight equivalent reproductively normal women [4]. This defect is independent of but considerably deteriorated by obesity. In contrast, hepatic IR, characterized by both excess postabsorptive glucose production and decreased sensitivity to insulin leading to suppression of endogenous glucose production, is existing only in obese women with PCOS related to control women of comparable body weight [2]. This synergistic deleterious influence of obesity and PCOS on endogenous glucose production may be a major factor in the pathogenesis of glucose intolerance [5].

Omentin is a fat depot-specific secretory protein produced by visceral stromal vascular cells, but not adipocytes. Omentin improved insulin-stimulated glucose transport and protein kinase B (Akt) phosphorylation in human subcutaneous and visceral adipocytes, proposing that omentin may improve insulin sensitivity [6]. Plasma omentin-1 levels, the major circulating isoform in human plasma, were related inversely with obesity and insulin resistance as determined by homeostasis model assessment yet correlated positively with adiponectin and HDL levels [7].

The objectives of this study were: to assess the serum omentin-1 concentration in PCOS women and the effect of Metformin on omentin-1 level, to evaluate the role of omentin-1 on IR and hyperandrogenemia in PCOS women and to study the correlation of omentin-1 with body mass index (BMI) in PCOS women.

Methods

This case control, nonrandomized study was conducted for evaluation of PCO patients who attended the High Institute for Infertility Diagnosis and Assisted Reproductive Technologies. The study was approved by the Institution Review Board of the College of Medicine, Al-Nahrain University, and written consent was obtained from patients. The study was extended from November 2015 to March 2016.

Eighty women involved in the study who were arranged in groups: 40 infertile women with PCOS constituted this group as a patient group, which is subdivided into four subgroups:

1) Group 1a: comprised 10 obese (BMI ≥30 kg/m^2) PCOS patient taking metformin 500 mg twice daily for the last three months.
2) Group 1b: included 10 obese (BMI ≥30 kg/m^2) PCOS patient not taking metformin for the last 3 months.
3) Group 1c: comprised ten non-obese (BMI <30 kg/m^2) PCOS patient taking metformin 500 mg twice daily for the last 3 months.
4) Group 1d: included ten non-obese (BMI <30 kg/m^2) PCOS patient not taking metformin for the last 3 months.

Forty apparently normal women considered as a control group, who were free from PCOS; they were further subdivided into two groups depending on the BMI into:

1) Group 2a: consist of twenty obese subjects with BMI ≥30 kg/m^2
2) Group 2b: encompassed twenty non-obese subjects with BMI <30 kg/m^2.

Inclusion criteria

1. Age between 18-35 years.
2. Have no other endocrine disease.

Exclusion Critera

1. Hyperprolactinemia
2. History of type II diabetes mellitus
3. Women with history of gestational diabetes mellitus

The following features were noted: menstrual history; presence of acne; hirsutism; BMI; a diagnosis of polycystic ovaries on ultrasound was based on the presence of 12 or more follicles measuring 2-9 mm and/or ovarian volume measuring >10 cm^3 [8]. The cases were examined by consultant physician in the infertility institute. Hirsutism is based on the

visual scoring method described by modified Ferriman and Gallwey scale. Nine body areas examined: upper lip, chin, chest, upper back, lower back, upper abdomen, lower abdomen, the upper arms and the thighs, hair growth is rated from 0 (no growth of terminal hair) to 4 (extensive hair growth) in each of the nine locations. A patient's score may therefore range from a minimum score of 0 to a maximum score of 36 cut-off value ≥6-8 [9].

The following parameters and biochemical measurements were done for the all subjects included in this study:

BMI assessment

it is equal to mass (kg)/ (height (m))^2. Obese (BMI ≥30 kg/m^2) and non-obese (BMI <30 kg/m^2).

Biochemical tests

Fasting blood glucose (FBG)

The examined individuals should be fasting for at least 12 hours prior to the test. three ml of venous blood samples were aspirated transferred into clean, plain tubes and centrifuged within 30 minutes of collection. Then the serum from all blood samples were separated; sugar was measured using enzyme colorimetric methods and the rest were stored at -20 °C.

Hormonal assay

1) Serum omentin.
2) Serum insulin.

Omentin was measured by using an omentin enzyme immunoassay or ELISA kit (Elabscience), according to the manufacturer's instructions.

Insulin hormone was measured by using an insulin enzyme immunoassay or ELISA kit (Calbio tech, Insulin Elisa), according to the manufacturer's instructions.

Homa insulin resistance also measured, which defined as fasting insulin (µIU/L) x Fasting glucose (mg/dL) / 405. HOMA score was < 3 considered normal, between 3 and 5 moderate IR and >5 severe IR [10].

Results

Omentin-1 level of group 1a was significantly lower than that of group 1c (P value = 0.01). On the contrary insulin level show significant increase in group 1a in comparison with group 1c (P value = 0.002), moreover, IR was significantly increased in group 1a in comparison with group 1c (P value = 0.001) (Table 1). While no significant differences were noticed in FBS level and hirsutism score (Tables 1 and 2)

Omentin-1 level of group 1a was significantly lower than that of group 1c (P value = 0.01). On the contrary insulin level show significant increase in group 1a in comparison with group1c (P value = 0.002), moreover, IR was significantly increased in group 1a in comparison with group 1c (P value = 0.001), (Table 3).

No significant differences were noticed in FBS level and hirsutism score (Tables 3 and 4).

Table (5) showed that insulin level, insulin resistance and FBS were significantly decreased in the control group as a whole when compared to PCOS patient without metformin treatment (P=0.02; 0.01; 0.02, respectively). On the contrary omentin-1 level was not different between the two groups.

Moreover, hirsutism score of PCOS group showed a significant increase in comparison to control group (P value = 0.01), furthermore those ≥ 6 in same group also showed a significant increase in comparison to control group (P value = 0.01) (Table 6).

Table 1. Comparison between patients with polycystic ovary syndrome without metformin treatment groups by unpaired t-test

Parameter	PCOS patients without metformin treatment		P value
	Obese N=10	Non-obese N=10	
Body weight (kg)	92.5±10.32	62.1±11.53	< 0.0001
Fasting blood sugar (mg/dl)	92.7±6.2	88.6±8.81	0.2444
Serum Insulin (µIU/ml)	20.38±10.55	9.29±6.73	0.0118
Serum Omentin (ng/ml)	1.61±0.84	2.52±1.39	0.0929
Insulin resistance	4.64±2.39	2.06±1.46	0.0093

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 2. Comparison of hirsutism between obese and non-obese patients with polycystic ovary syndrome by Fisher exact test

Parameter	PCOS patients without metformin treatment		P value
	Obese N=10	Non-obese N=10	
< 6	7 (70)	9 (90)	0.582
≥ 6	3 (30)	1 (10)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

Table 3. Comparison between obese and non-obese PCOS with metformin treatment groups by unpaired t-test

Parameter	PCOS patients with metformin treatment		P value
	Obese N=10	Non-obese N=10	
Body weight (kg)	86.8±9.86	67.7±10.09	0.0004
Fasting blood sugar (mg/dl)	95.7±4.08	90.8±6.83	0.0672
Serum Insulin (µIU/ml)	9.66±5.88	2.77±1.44	0.0021
Serum Omentin (ng/ml)	1.59±1.48	3.02±0.71	0.0132
Insulin resistance	2.27±1.34	0.61±0.29	0.0012

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 4. Comparison of hirsutism between obese and non-obese PCOS on metformin treatment by Fisher exact test

Parameter	PCOS patients with metformin treatment		P value
	Obese N=10	Non-obese N=10	
< 6	6 (60)	6 (60)	1.000
≥ 6	4 (40)	4 (40)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

Table 5. Comparison between control group and PCOS group without metformin treatment by unpaired t-test

Parameter	Control N=40	PCOS patients without metformin treatment N=20	P value
Body weight (kg)	72.08±15.28	77.3±18.88	0.2909
Fasting blood sugar (mg/dl)	84.73±10.62	90.65±7.71	0.0173
Serum Insulin (µIU/ml)	8.38±7.28	14.84±10.32	0.0183
Serum Omentin (ng/ml)	1.73±1.49	2.07±1.21	0.3508
Insulin resistance	1.78±1.55	3.35±2.33	0.0111

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 6. Comparison of hirsutism between obese and non-obese PCOS on metformin treatment by Fisher exact test

Parameter	Control N=40	PCOS patients without metformin treatment N=20	P value
< 6	40 (100)	16 (80)	0.010
≥ 6	0 (0)	4 (20)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

There was significant decrease in FBS of control group in comparison with PCOS group (on metformin treatment) (P value = 0.0002). No significant differences were noticed in omentin, insulin levels and insulin resistance, BMI (Table 7).

Hirsutism score of PCOS group on metformin treatment < 6 showed a significant increase in comparison to control group (P value =0.001). Furthermore, those ≥ 6 in same group also showed a significant increase (8 in comparison to control group (P value = 0.001) (Table 8).

The insulin level and IR were significantly increased in PCOS patients without metformin treatment versus those on metformin treatment (P=0.002; P=0.003, respectively), (Table 9).

No significant differences were noticed in FBS, omentin level, BMI and hirsutism score (Tables 9 and 10).

Table 7. Comparison between control group and PCOS group with metformin treatment by unpaired t-test

Parameter	Control N=40	PCOS patients with metformin treatment N=20	P value
Body weight (kg)	72.08±15.28	77.25±13.8	0.1937
Fasting blood sugar (mg/dl)	84.73±10.62	93.25±6.03	0.0002
Serum Insulin (µIU/ml)	8.38±7.28	6.21±5.47	0.2027
Serum Omentin (ng/ml)	1.73±1.49	2.31±1.35	0.1397
Insulin resistance	1.78±1.55	1.44±1.27	0.3729

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 8. Comparison of hirsutism between control group and PCOS group with metformin treatment by Fisher exact test

Parameter	Control N=40	PCOS patients with metformin treatment N=20	P value
< 6	40 (100)	12 (60)	0.001
≥ 6	0 (0)	8 (40)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

Table 9. Comparison between PCOS patients on metformin and those without metformin treatment by unpaired t-test

Parameter	PCOS patients		P value
	Without metformin treatment N=20	With metformin treatment N=20	
Body weight (kg)	77.3±18.88	77.25±13.8	0.9924
Fasting blood sugar (mg/dl)	90.65±7.71	93.25±6.03	0.2420
Serum Insulin (µIU/ml)	14.84±10.32	6.21±5.47	0.0021
Serum Omentin (ng/ml)	2.07±1.21	2.31±1.35	0.5604
Insulin resistance	3.35±2.33	1.44±1.27	0.0027

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 10. Comparison of hirsutism between PCOS group without metformin treatment and PCOS group with metformin treatment by Fisher exact test

Parameter	PCOS patients		P value
	Without metformin treatment N=20	With metformin treatment N=20	
< 6	16 (80)	12 (60)	0.301
≥ 6	4 (20)	8 (40)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

Insulin level was highly significantly decreased in group 2a in comparison with group 1b (P value =0.02). IR of group 2a was significantly lower than that of group 1b (P value = 0.01). No significant differences were noticed in, FBS, omentin level (Table 11).

Hirsutism score of group 1b < 6 showed a significant increase in comparison to group 2a (P value = 0.03), furthermore, those ≥ 6 in same group also showed a significant increase in comparison to group 2a (P value =0.03) (Table (12).

Table 11. Comparison between obese control group and obese PCOS group without metformin treatment by unpaired t-test

Parameter	Obese Control N=20	Obese PCOS patients without metformin treatment N=10	P value
Body weight (kg)	83.75±10.47	92.5±10.32	0.0426
Fasting blood sugar (mg/dl)	86.5±11.56	92.7±6.2	0.0664
Serum Insulin (µIU/ml)	10.38±8.01	20.38±10.55	0.019
Serum Omentin (ng/ml)	1.5±1.32	1.61±0.84	0.7702
Insulin resistance	2.27±1.78	4.64±2.39	0.0148

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 12. Comparison of hirsutism between PCOS group without metformin treatment and PCOS group with metformin treatment by Fisher exact test

Parameter	Obese Control N=20	Obese PCOS patients without metformin treatment N=10	P value
< 6	20 (100)	7 (70)	0.030
≥ 6	0 (0)	3 (30)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

FBS of group 2a was significantly lower than that of group 1a (P value =0.003) (Table 13). No significant differences were noticed in insulin, omentin, BMI and insulin resistance.
Hirsutism score of group 1a < 6 showed a significant increase in comparison to control group 2a (P value =0.008), furthermore those ≥ 6 in same group also showed a significant increase in comparison to control group (P value <0.008) (Table 14).

Table 13. Comparison between obese control group and obese PCOS group with metformin treatment by unpaired t-test

Parameter	Obese Control N=20	Obese PCOS patients with metformin treatment N=10	P value
Body weight (kg)	83.75±10.47	86.8±9.86	0.4437
Fasting blood sugar (mg/dl)	86.5±11.56	95.7±4.08	0.0037
Serum Insulin (µIU/ml)	10.38±8.01	9.66±5.88	0.7827
Serum Omentin (ng/ml)	1.5±1.32	1.59±1.48	0.8657
Insulin resistance	2.27±1.78	2.27±1.34	0.9982

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 14. Comparison of hirsutism between obese control group and obese PCOS group with metformin treatment by Fisher exact test

Parameter	Obese Control N=20	Obese PCOS patients with metformin treatment N=10	P value
< 6	20 (100)	6 (60)	0.008
≥ 6	0 (0)	4 (40)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

Omentin level in group 2b was significantly lower than that of group 1c (P value = 0.02). Insulin level show highly significant increase group 2b in comparison group1c (P value = 0.02). Insulin resistance of group 2b was also significantly higher than Insulin resistance of group1c (P value = 0.02). On the reverse, FBS shows significant decrease group2b in comparison with group1c (P value = 0.02), (Table 15). No significant difference was noticed in BMI. Moreover, hirsutism score of group1c < 6 showed a significant increase in comparison to group2b (P value < 0.008), furthermore those ≥ 6 in same group also showed a significant increase in comparison to group2b (P value < 0.008) (Table 16).
Table (17) illustrates a significant negative correlation between omentin and BMI in patients of group1a and 1c (r = -0.472, P value = 0.035).
There was no significant correlation in fasting blood sugar, serum insulin and insulin resistance and hirsutism score among these groups.

Table 15. Comparison between non-obese control group and non-obese PCOS group on metformin treatment by unpaired t-test

Parameter	Non-obese Control N=20	Non-obese PCOS patients with metformin treatment N=10	P value
Body weight (kg)	60.4±9.09	67.7±10.09	0.071
Fasting blood sugar (mg/dl)	82.95±9.55	90.8±6.83	0.0162
Serum Insulin (µIU/ml)	6.39±6.03	2.77±1.44	0.0183
Serum Omentin (ng/ml)	1.96±1.65	3.02±0.71	0.021
Insulin resistance	1.29±1.13	0.61±0.29	0.0192

The data presented in mean±SD, PCOS = Polycystic ovary syndrome

Table 16. Comparison of hirsutism score between non-obese control group and non-obese PCOS group on metformin treatment by Fisher exact test

Parameter	Obese Control N=20	Non-obese PCOS patients with metformin treatment N=10	P value
< 6	20 (100)	6 (60)	0.008
≥ 6	0 (0)	4 (40)	

The data presented with number and percentage, PCOS= polycystic ovary syndrome

Table 17. Correlation of omentin with body mass index, Fasting blood Sugar, Serum Insulin, Insulin resistance and Hirsutism score

Parameter	Control N=40		PCOS without metformin treatment N=20		PCOS on metformin treatment) N=20	
	r	p	r	p	r	p
BMI (kg/m^2)	-0.090	0.582	-0.270	0.250	-0.472	0.035
Fasting blood Sugar	-0.029	0.859	0.291	0.213	-0.441	0.052
Serum Insulin	0.176	0.278	-0.118	0.622	0.053	0.823
Insulin resistance	0.129	0.429	-0.080	0.739	0.014	0.952
Hirsutism score	-	-	0.237	0.315	0.163	0.494

PCOS= polycystic ovary syndrome

Discussion

Omentin-1 lipoprotein is a newly discovered adipokine mediator as it is released from visceral stromal mesenchymal vascular tissue fatty and non-fatty cells and its release in plasma is act as a bi-product of lipid metabolism (anabolic and catabolic pathways) as in lipid peroxidation. It has prospect values

in management of certain endocrine disorders like DM type2 and polycystic ovary and its relation to insulin resistance level in patients with polycystic ovary syndrome [11].

The state of hyperinsulinemia may itself contribute to obesity by the anabolic effect of insulin on fat metabolism through adipogenesis via increased uptake of glucose into adipocytes, which eventually leading to the production of triglycerides and inhibition of hormone sensitive lipase [12]. While other researchers found that IR in PCOS may lead to low energy expenditure, where those women appear to have significantly lower basal metabolic rate than do age- and BMI-matched controls (1446 kcal/day versus 1841 kcal/day). Although many patients with PCOS have IR independent of obesity, the obesity worsens underlying IR and insulin resistance-associated reproductive and metabolic effects [13].

In the present study, there is significant difference between the hirsutism score in PCOS patient and control subjects. This is agreed with Sirmans et al. [14] who reported that PCOS is a common heterogeneous endocrine disorder characterized by irregular menses, hyperandrogenism, and hirsutism in addition to polycystic ovaries, suggesting that a primary defect in androgen metabolism is the intrinsic, major factor in the pathogenesis of PCOS [15].

Current study found that there is no significant difference in serum omentin-1 level between non-obese PCO without metformin treatment in comparison with non-obese control group, this is in agreement with Akbarzadeh et al. [16] who proved that PCOS is not a determinant of decreased omentin plasma level may be due to high androgen level and IR as warning signs of PCOS. While in contradiction with Yang et al. [17] who reported significant decrease in plasma omentin level of non-obese PCO in comparison with healthy control, this may be due to larger sized sample (n=153 healthy group, 114 PCOS individuals) contributes to this controversy [16].

Furthermore, there is no significant difference in serum omentin-1 level between obese PCO without metformin treatment in comparison with obese control group, this concept in disagreement with Mahde et al. [18] who revealed that there is significant difference between obese PCO and control group, the differences in BMI of control group between their study (29.56 ± 2.12) and ours (33.38±3.7) may explain this discrepancy.

Metformin's main action is to decrease the overproduction of glucose by the liver, a common problem in prediabetes and type 2 diabetes. The action of metformin helps lower blood sugar levels particularly during the night to keep fasting glucose levels under control, but it also helps control blood glucose throughout the day. Metformin also increases the uptake of glucose by your muscles. Overall, metformin decreases IR and improves insulin sensitivity, thereby helping the insulin your body still makes work more effectively [19,20].

One of the main metabolic features of metformin is its ability to reduce hepatic glucose production [21]. A recent study suggested that inhibition of mitochondrial glycerophosphate dehydrogenase (mGPD), a critical enzyme in the glycerophosphate shuttle, could be the primary mechanism of metformin-induced inhibition of gluconeogenesis [22,23].

Other studies have shown that the intestines play a significant role in the glucose-lowering effect of metformin by facilitating uptake and utilization of glucose [24].

This study concluded that serum omentin-1 level is decreased remarkably with increasing body weight in PCOS. Also, non-obese PCOS respond better to metformin treatment than obese PCOS in enhancing insulin sensitivity and in increasing serum omentin-1 concentration. Furthermore, this study showed no effect of serum omentin-1 level on insulin resistance and hyperandrogenism.

This study recommends to do a research on larger sized groups to ensure more precise prediction of changes in different variables. Also recommends doing a paired study (before and after taking metformin) is advisable to be in account than unpaired study in further

researches. Longer duration (>3 months) of metformin treatment is as well recommended to achieve better results regarding omentin-1 effect in PCOS patients.

Acknowledgments
The authors are deeply indebted to the members of the Department of Physiology and Medical Physics, College of Medicine/Al-Nahrain University, Dr. Abbas Fadhel, Dr. Majid Hameed, for their encouragement, advice and unforgettable help. Also authors express thanks and respect to all the staff of High Institute for Infertility Diagnosis and Assisted Reproductive Technologies.

Authors Contribution:
Dr. Kareem conducted the study, collected the data and performed the statistical analysis and drafting the manuscript. Dr. Hashim contributed in the designing, organization and finalization of manuscript. Dr. Almoayed: referring the PCOS cases.

Conflict of interest
The authors declare no conflict of interest.

Funding
Self-funding.

References
1. Sam S, Dunaif A. Polycystic ovary syndrome: syndrome XX. Trends Endocrinol Metab. 2003; 14(8): 365-70.
2. Sam S. Obesity and polycystic ovary syndrome. Obes Manag. 2007; 3(2): 69-73. doi: 10.1089/obe.2007.0019.
3. Chiu HK, Tsai EC, Juneja R, et al. Equivalent insulin resistance in latent autoimmune diabetes in adults (LADA) and type 2 diabetic patients. Diabetes Res Clin Pract. 2007; 77: 237-44. doi: 10.1016/j.diabres.2006.12.013.
4. Hoffman L, Ehrmann DA. Genetic considerations in the evaluation of menstrual cycle irregularities. In: Weiss RE, Refetoff S. (eds.) Genetic diagnosis of endocrine disorders. London: Academic Press; 2010. p. 207-215.
5. Palioura E, Diamanti-Kandarakis E. Industrial endocrine disruptors and polycystic ovary syndrome. J Endocrinol Invest. 2013; 36(11): 1105-11. doi: 10.1007/BF03346762.
6. Yang RZ, Lee MJ, Hu H, et al. Identification of omentin as a novel depot-specific adipokine in human adipose tissue: possible role in modulating insulin action. Am J Physiol Endocrinol Metab. 2006; 290(6): E1253-61. doi: 10.1152/ajpendo.00572.2004.
7. de Souza Batista CM, Yang RZ, Lee MJ, et al. Omentin plasma levels and gene expression are decreased in obesity. Diabetes. 2007; 56(6): 1655-1661. doi: 10.2337/db06-1506.
8. Huang A, Brennan K, Azziz R. Prevalence of hyperandrogenemia in the polycystic ovary syndrome diagnosed by the National Institutes of Health 1990 criteria. Fertil Steril. 2010; 93(6): 1938-41. doi: 10.1016/j.fertnstert.2008.12.138.
9. Yildiz BO, Bolour S, Woods K, et al. Visually scoring hirsutism. Hum Reprod Update. 2010; 16(1): 51-64. doi: 10.1093/humupd/dmp024.
10. Kelly AS, Bergenstal RM, Gonzalez-Campoy JM, et al. Effects of Exenatide vs. Metformin on endothelial function in obese patients with pre-diabetes: a randomized trial. Cardiovasc Diabetol. 2012; 11: 64. doi: 10.1186/1475-2840-11-64.
11. Choi JH, Rhee EJ, Kim KH, et al. Plasma omentin-1 levels are reduced in non-obese woman with normal glucose tolerance and polycystic ovary syndrome. Eur J Endocrinol. 2011; 165(5): 789-96. doi: 10.1530/EJE-11-0375.
12. Barber TM, McCarthy MI, Wass JA, et al. Obesity and polycystic ovary syndrome. Clin Endocrinol (Oxf) 2009; 65(2): 137-45. doi: 10.1111/j.1365-2265.2006.02587.x.
13. Georgopoulos NA, Saltamavros AD, Vervita V, et al. Basal metabolic rate is decreased in women with polycystic ovary syndrome and biochemical hyperandrogenemia and is associated with insulin resistance. Fertil Steril. 2009;92(1):250-5. doi: 10.1016/j.fertnstert.2008.04.067.
14. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. Clin Epidemiol. 2014; 6: 1-13. doi: 10.2147/CLEP.S37559.
15. Escobar-Morreale HF, Alvarez-Blasco F, Botella-Carretero JI, et al. The striking similarities in the metabolic associations of female androgen excess and male androgen deficiency. Hum Reprod. 2014; 29(10): 2083-91. doi: 10.1093/humrep/deu198.
16. Akbarzadeh S, Ghasemi S, Kalantarhormozi M, et al. Relationship among plasma adipokines, insulin and androgens level as well as biochemical glycemic and lipidemic markers with incidence of PCOS in women with normal BMI. Gynecol Endocrinol. 2012; 28(7): 521-4. doi: 10.3109/09513590.2011.650747.
17. Yang HY, Ma Y, Lu XH, et al. The correlation of plasma omentin-1 with insulin resistance in non-obese polycystic ovary syndrome. Ann Endocrinol (Paris). 2015; 76(5): 620-7. doi: 10.1016/j.ando.2015.08.002.
18. Mahde A, Shaker M, Al-Mashhadani Z. Study of omentin1 and other adipokines and hormones in PCOS patients. Oman Med J. 2009; 24(2): 108-18. doi: 10.5001/omj.2009.25.
19. Pasquali R, Gambineri A, Biscotti D, et al. Effect of long-term treatment with metformin added to hypocaloric diet on body composition, fat distribution, and androgen and insulin levels in

abdominally obese women with and without the polycystic ovary syndrome. J Clin Endocrinol Metab. 2000; 85(8): 2767-74. doi: 10.1210/jcem.85.8.6738.

20. Sloane S. Metformin: improving insulin sensitivity. Diabetic living: Reviewed 2014. (http://www.diabeticlivingonline.com/medication/oral/metformin-improving-insulin-sensitivity). Accessed may 16th 2016).

21. Madiraju AK, Erion DM, Rahimi Y, et al. Metformin suppresses gluconeogenesis by inhibiting mitochondrial glycerophosphate dehydrogenase. Nature. 2014; 510(7506): 542-6. doi: 10.1038/nature13270.

22. Hinke SA, Martens GA, Cai Y, et al. Methyl succinate antagonises biguanide-induced AMPK-activation and death of pancreatic beta-cells through restoration of mitochondrial electron transfer. Br J Pharmacol. 2007; 150: 1031-43. doi: 10.1038/sj.bjp.0707189.

23. Derrien M, Van Baarlen P, Hooiveld G, et al. Modulation of Mucosal Immune Response, Tolerance, and Proliferation in Mice Colonized by the Mucin-Degrader Akkermansia muciniphila. Front Microbiol. 2011; 2: 166. doi: 10.3389/fmicb.2011.00166.

24. Lee H, Ko G. Effect of metformin on metabolic improvement and gut microbiota. Appl Environ Microbiol. 2014; 80(19): 5935-43. doi: 10.1128/AEM.01357-14.

Correspondence to Dr. Jumana M. Kareem
E-mail: jumana86.jm@gmail.com
dr_jumana.jm@colmed-alnahrain.edu.iq
Received Jan. 3rd 2017
Accepted Apr. 24th 2017