# Serum Visfatin in Iraqi Women with Polycystic Ovary Syndrome

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**Abstract**

Visfatin is a peptide that is predominantly expressed and secreted from adipose tissue and exerts insulin-mimicking effects through activation of an insulin receptor. The aim of this study to evaluated serum visfatin level in both lean and obese Polycystic Ovary Syndrome (PCOS) subjects before and after treatment with metformin . This study included (80) women, 20 lean with PCOS (BMI <25 kg $m^{-2}$) **(group A)** while (**group B)** include 20 obese with PCOS (BMI >30 kg $m^{-2}$) and **(group C)** include 40 healthy normally menstruating women (20 lean and 20 obese) are control**.** All these groups were detected after treatment with metformin for 3 months. Metformin was given at doses up to 1500 mg/day for three month; the patients with polycystic ovary syndrome were attended to obstetrics and gynecology outpatient and primary health care outpatient in Al – Yarmouk Teaching Hospital, and Kamal-Al-Samaraae Hospital. The control subjects were recruited mainly from medical students and staff. Serum visfatin was estimated before and after treatment.

A results showed that significant high increase in mean serum visfatin level in lean polycystic ovary syndrome compared to control lean (6.35±1.07 ng/ml versus 0.26±0.11 ng/ml, P=0.0001*) ,and also in obese polycystic ovary syndrome showed a significant increase compared to control obese(1.31±0.39 ng/ml versus 0.29±0.08 ng/ml, P=0.0001*). Serum visfatin was reduced in both lean and obese polycystic ovary syndrome after treatment with metformin.

By this study, we can conclude Serum Visfatin level increased in polycystic ovary syndrome groups and this increment is high in lean group. These findings might suggest that visfatin could play a role in pathogenesis of polycystic ovary syndrome. Metformin decrease serum visfatin level in both lean and obese groups.

**Key Words:** Visfatin, Polycystic Ovary Syndrome**.**

## Introduction:

Polycystic ovary syndrome is one of the most common female endocrine disorders affecting women at reproductive age (12–45 years old) and is thought to be one of the leading causes of female infertility [(1)]**.** The Rotterdam criteria expanded the definition to diagnose women with PCOS if they have two of the following characteristics: -

(i) Oligo- and/or an ovulation.
(ii) Clinical and/or biochemical signs of hyperandrogenism.
(iii) Polycystic ovary morphology on ultrasound scan is defined by the presence of 12 or more follicles measuring 2-9mm in diameter in any one ovary or increased ovarian volume >10$cm^3$ [(2)]**.** An estimate of PCOS in the community suggests a prevalence of17.8 % using the Rotterdam criteria [(3)].The pathophysiology of PCOS is complex and highly debatable with environmental and constitutional defects [(4)].

Visfatin is an adipokine identified in 2004and thus named for the suggestion that it would be predominantly produced and secreted in visceral fat. (Visceral fat adipokine) [5]. visfatin is an endocrine, autocrine as well as paracrine protein with many functions, including enhancement of cell proliferation, biosynthesis of nicotinamide mono- and dinucleotide and insulin mimetic (Hypoglycaemic effect)[6] .Visfatin concentrations are increased in patients with type two diabetes mellitus (T2DM). Due to the similar characteristics of diabetes and PCOS, it has been proposed that visfatin may play a role in the pathogenesis of insulin resistance and hyperinsulinemia seen in many of these women [7].

Metformin is an oral hypoglycemic agent that is used for lowering insulin and blood sugar levels in women with polycystic ovary syndrome (PCOS). This helps in regulating menstrual cycles, start ovulation, and lower the risk of miscarriage in women with PCOS. Also long-term use lowers risk of diabetes and heart disease related to high insulin levels [8].

The aim of this study to evaluated serum visfatin level in both lean and obese polycystic ovary syndrome (PCOS) subjects before and after treatment with metformin

## Material and Methods:

The study included (80) women, 20 lean with PCOS (BMI <25 kg $m^{-2}$) **(group A)** while (**group B)** include 20 obese with PCOS (BMI >30 kg $m^{-2}$) and **(group C)** include40 healthy normally menstruating women (20 lean and 20 obese) are control**.** All these groups were detected after treatment with metformin for 3 months. Ethical consent was obtained and written from each patient during the study, under the approval of ministry of health. The patients with PCOS were attended to obstetrics and gynecology outpatient and primary health care outpatient in Al –Yarmouk Teaching Hospital, and Kamal-Al-Samaraae Hospital.

The diagnosis of polycystic ovary syndrome (PCOS) was established according to Rotterdam criteria (oligo- and/or an ovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries in ultrasonography (USG) scan as well as exclusion of other etiologies which mimics the PCOS phenotype.

The exclusion criteria were: Pharmacological treatment in the preceding 12 weeks , Breast feeding in the preceding 24 weeks ,Cardiovascular disease, Diabetes(fasting glucose 125 mg/dl), Morbid obesity (BMI 40 kg $m^{-2}$),Other endocrine disorders, such as congenital adrenal hyperplasia, Cushing´s syndrome or androgen-secreting tumors.

The Body Mass Index is a measure of body weight relative to height which is defined as the individual's body weight divided by the square of her height. Venous blood was taken from each individual at time 8-11a.m, while patients were after an overnight fast and on follicular phase ($2^{nd}$ or $3^{rd}$) day of menses.

Serum visfatin was determined by an enzyme immunoassay for quantitative in vitro diagnostic measurement using kit Manufactured by **(**Biovision Catalog #K4907)

## Results and Discussion:

For data encoding and analysis; SPSS (statistical package for social science version 16.0, SPSS Inc. Chicago, Illinois, USA) was used and the test of significance association was done by one way ANOVA tests and the cutoff point of significance was (< 0.05) P value. This study showed a significant high increase in mean serum Visfatin level in lean PCOS compared to control lean (6.35±1.07 ng/ml versus 0.26±0.11 ng/ml, P=0.0001*) ,and also in obese PCOS showed a significant increase compared to control obese(1.31±0.39 ng/ml versus 0.29±0.08 ng/ml, P=0.0001*) as show in Figure (1) and Table (1).

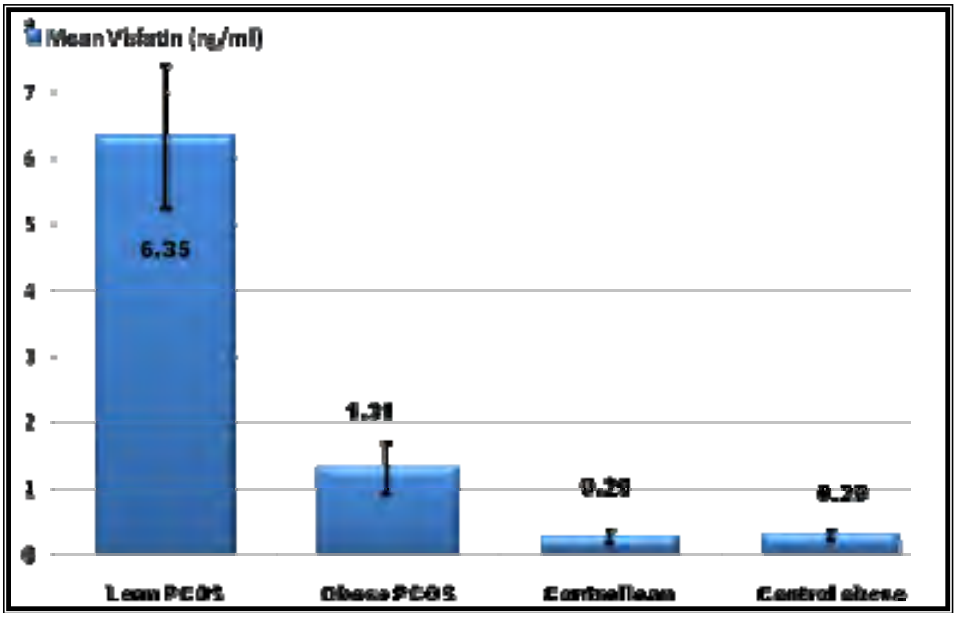


Fig. (1): Mean of serum Visfatin level in all studied groups before treatment

Table (1): Comparison of serum Visfatin level between all studied groups before treatment

| Visfatin before treatment (ng/ml) | Lean PCOS | Obese PCOS | Control lean | Control obese |
|---|---|---|---|---|
| Mean ±SD | 6.35±1.07 | 1.31±0.39 | 0.26±0.11 | 0.29±0.08 |
| Standard Error of Mean | 0.24 | 0.09 | 0.04 | 0.03 |
| Range | 4.7-8.0 | 0.5-2.0 | 0.1-0.5 | 0.2-0.4 |
| P value compared to Lean PCOS | - | 0.0001* | 0.0001* | 0.0001* |
| Obese PCOS | - | - | 0.0001* | 0.0001* |
| Control lean | - | - | - | 0.972 |

After treatment with metformin serum visfatin level was reduced in both lean and obese PCOS as shown as in Table and Figure (**2**).

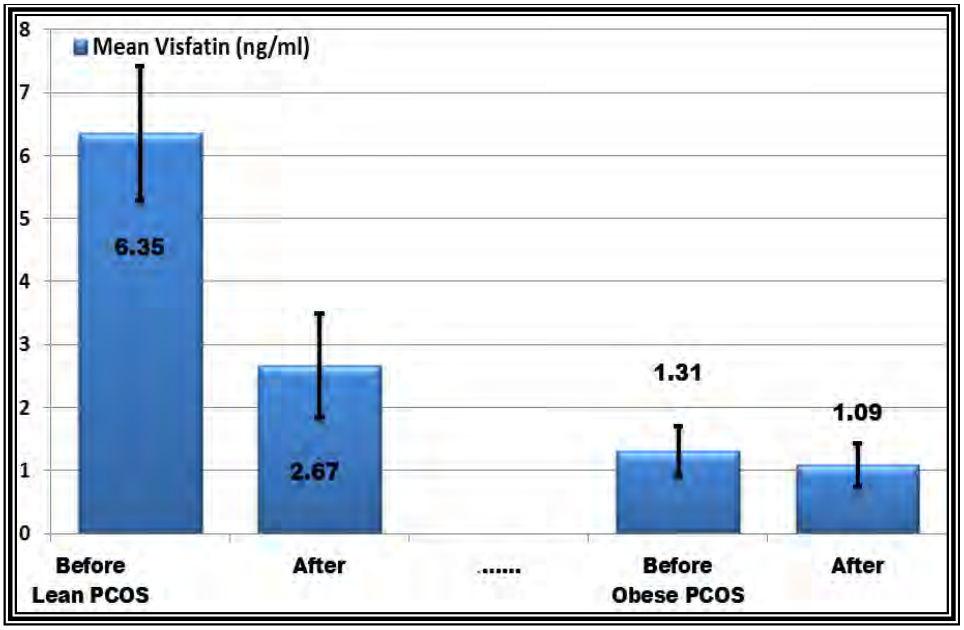


Fig. (2): Mean of serum Visfatin level in both lean and obese groups after treatment

Table (2): Serum Visfatin level in both lean and obese PCOS after Treatment

| Visfatin (ng/ml) | Lean PCOS | | Obese PCOS | |
|---|---|---|---|---|
| | BEFORE | AFTER | BEFORE | AFTER |
| Mean±SD | 6.35±1.07 | 2.67±0.82 | 1.31±0.39 | 1.09±0.34 |
| Standard Error of Mean | 0.24 | 0.26 | 0.09 | 0.11 |
| Range | 4.7-8.0 | 1.9-4.0 | 0.5-2.0 | 0.7-1.7 |
| Paired t-test | 0.0001* | | 0.0001* | |
| P value compared to Lean PCOS | - | | 0.0001* | 0.0001* |

**Serum visfatin correlations with all studied variable**

Table (3): Correlations and P-Value of serum visfatin with all studied parameters

| | | **Visfatin (ng/ml)** | | | |
|---|---|---|---|---|---|
| | | **Lean PCOS** | **Obese PCOS** | **Lean control** | **Obese control** |
| **Age (years)** | **r** | **-0.023** | **0.197** | **-0.262** | **0.186** |
| | **P** | **0.925** | **0.404** | **0.496** | **0.631** |
| **BMI (Kg/m2)** | **r** | **0.011** | **-0.429** | **0.153** | **-0.471** |
| | **P** | **0.964** | **0.059** | **0.695** | **0.201** |

## Discussion:

In the present study, there was an increased in serum visfatin concentration of PCOS women. These findings might suggest that visfatin could play a role in pathogenesis of PCOS. In previous studies, authors did not found a relation between circulating visfatin concentration and insulin action**.** Therefore, one might suppose that the correlation observed in our study might be due to the inclusion of these specific clinical group patients with PCOS. Researchers reported an increase in serum visfatin concentration in different insulin resistant conditions, such as type 2 diabetes[)]**,** morbid obesity, or gestational diabetes[)]**,** although opposing observations were also reported. While in this study we measure the serum visfatin in both lean and obese PCOS women and matched controls because women with PCOS have an increased prevalence of visceral obesity and the metabolic syndrome, and it was found that the PCOS groups had significantly higher serum visfatin concentrations (6.35±1.07 ng/ml), and (1.31±0.39 ng/ml) in lean and obese respectively, which has been supported elsewhere in the previous studies**.** The rationale for the increased levels of plasma visfatin in women with PCOS is still being explored, but a few concepts have been suggested. Previous studies in 2006 suggested that the increased visfatin levels seen in PCOS patients may be due to either impaired visfatin signaling in target tissues, an overall dysregulation in visfatin biosynthesis, compensatory response in insulin resistant tissues and visfatin as a marker of tissue-specific inflammatory cytokine action [(14)].A study in 2007 supported the first two suggestions as causes for increased levels in patients with T2DM [(17)]**,** which has led to further study regarding the impact of increased visfatin concentration as a possible contributor to insulin resistance in PCOS. The insulin-mimetic properties of visfatin, as well as the potential associations between visfatin and insulin resistance, present a potential role of visfatin in the pathogenesis of the insulin resistance seen in women with PCOS [(17)]. The release of visfatin by adiposities was dependent on duration and magnitude of glucose elevation **.**Several studies has recorded the use of metformin in women with PCOS. Metformin is effective in reducing testosterone levels and in making the menstrual cycle more regular. While metformin starts to improve the prospects for fertility in few weeks, a reduction in unwanted hair growth would be expected to take some months and be slower than conventional treatment [(18)]**.**Adipose tissue is not a major site of metformin's action; however metformin appears to have modest effects on this tissue. An older in vitro study has examined how metformin affects metabolic pathways in pre adiposities; metformin was shown to stimulate catabolism, as reflected by increases in glucose transport and utilization, mitochondrial and peroxisomal fatty acid β-oxidation, basal lipolysis, and aerobic and anaerobic respiration. These effects were all independent of insulin. The caveat is that findings in preadipocytes cannot be safely extrapolated to mature adiposities.

## Conclusion:

We can find in this study women can lose weight easier when taking metformin even though it is not a traditional weight reducing agent. Also induce ovulation as found by one placebo-controlled trail has that shown metformin is better than placebo in inducing ovulation in women with PCOS

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