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# Adipocytokine Visfatin in patients with polycystic ovary syndrome

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## Abstract

**Background**: Visfatin, a protein secreted by adipose tissue, is suggested to play a role in the pathogenesis of insulin resistance. In polycystic ovary syndrome (PCOS), insulin resistance might be involved in the development of endocrine and metabolic abnormalities .Polycystic ovary syndrome (PCOs), is a common endocrine disorder affecting up to 10% of women of reproductive age, is expressed as chronic anovulation and hyper-androgenism. High serum visfatin was found to be associated with insulin resistance and markers of hyper-androgenism in lean PCOS patients. **Objectives**: To assess plasma visfatin concentrations in women with polycystic ovary syndrome and its correlation with their BMI. **Subjects& methods**: visfatin, fasting glucose, fasting insulin, homeostasis model assessment (HOMA)-IR, cholesterol (total, HDL, LDL),triglyceride, LH/FSH ratio, and BMI, waist circumference were measured and pelvic ultrasound done in a group of 24 female with PCOS(12 lean,12 obese)and 20 healthy control(10 lean,10 obese). **Results**: as regard differences between lean and obese PCOS we found significant differences as regard visfatin, Fasting insulin , HOMA-IR, cholesterol, BMI and highly significance difference as regard LDL with no significant differences as regard, FBG,LH/FSH ratio ,TG. Also we found sig positive correlation (P<0.05) between visfatin &BMI, cholesterol, wt in lean PCOS and HOMA-IR, LH/FSH ratio in obese PCOS. C**onclusion:** we concluded that women with PCOS exhibit higher visfatin level, more in lean cases than obese PCOS and their control, also visfatin associated with insulin resistance state that accompany the obese PCOS.

**Keywords:** PCOS ; insulin resistance ; Visfatin.

## Introduction

PCOS is the most common endocrine disorder diagnosed in 5-10%of premenopausal women of reproductive age. Hyper-androgenemia, anovulation, and insulin resistance with accompanying hyperinsulinemia play a major role in the development of the signs and symptoms that are associated with PCOS (1).

Patients with PCOS show metabolic abnormalities combined with a more android type of adiposity than that found in normal subjects with similar BMI **(2).**
The difference in fat distribution in women with PCOS may result in changed adipose tissue function and adipokine levels (3).

Patients with PCOS display an impairment of insulin-stimulated glucose utilization in peripheral tissue (4), and frequently associated with central obesity, IGT, and T2DM (5).

Visfatin, a recently described new adipokine is abundantly produced by adipocytes and is also considered to link obesity with diabetes and insulin resistance. It has been demonstrated in cultured cells and in animal experiments that visfatin binds to the insulin receptor and exerts insulin action, and it is assumed that it induces the intracellular signaling cascade for insulin with tyrosine phosphorylation of the insulin receptor and its substrates (IRS1 and IRS2) and activation of protein kinase B activity (6**).**

Visfatin, found primarily in the cell nucleus and cytoplasm, lacks a signal sequence and is released during lipolysis (7)

It has been shown that visceral adipose tissue produces visfatin, which may regulate insulin sensitivity (6**),** higher plasma levels of visfatin in patients with type 2

diabetes mellitus and women with gestational diabetes mellitus have been found(8)(9)**.** On the basis of these observations, good support is given for the hypothesis that plasma visfatin concentrations would be higher in women with PCOS., and may suggest an impaired mechanism of visfatin signaling in target tissues in states of insulin resistance (10).

## Materials and Methods

This study was conducted on 44 subjects. They were divided into 2 main groups:

**Group (I)** included 24 female patients with polycystic ovary syndrome ,mean age ranged from (22-32 years), they were further subdivided into obese subgroup (BMI ≥ 30) and lean subgroup (BMI < 25) .Each subgroup was formed of 12 patients.

**The obese subgroup** contained 12 females (mean age25.25±3.19 years) and mean BMI 32.43±3.14 kg/m2, while **the lean subgroup** contained 12 females with a mean age of 25.08 ±2.35 years and BMI of 23.19±1.28kg/m².

**Group (II)** included 20 healthy subjects as a control group, this group was also further subdivided into 2 subgroups **obese** formed of 10 females with mean age 25.6±1.57years and mean BMI 31.254±0.71kg/m2 on the other side the **lean subgroup** consisted of 10 female subjects. Their mean age was 25.7±1.77 years while the mean of their BMI was 23.45±0.63kg/m².

**Table (1)** :descriptive data for the studied subgroups as regard clinical and laboratory parameters:

| | Obese PCOS mean±SD | Obese Control mean±SD | Lean PCOS mean±SD | Lean control mean±SD |
|---|---|---|---|---|
| Age (yrs) | 25.25±3.19 | 25.6±1.57 | 25.08 ±2.35 | 25.7±1.77 |
| Wt (kg) | 85.65±7.94 | 83.1±5.78 | 63.33±2.42 | 61.2±3.29 |
| Ht (m) | 1.62±0.03 | 1.63±0.04 | 1.56±0.03 | 1.615±0.04 |
| Visfatin | 79.25±6.85 | 58.8±8.22 | 86.08±6.35 | 59.7±12.42 |
| FPG(mg\dl) | 91.75±6.79 | 78.3±7.78 | 89.58±4.98 | 85.9±9.45 |
| Fasting plasma insulin(IU\ml) | 14.92±3.55 | 9.1±3.54 | 13.33±3.47 | 8±1.63 |
| HOMA | 3.31±0.69 | 1.592±0.53 | 3.00±0.72 | 1.662±0.22 |
| LH(mIu\ml) | 12.83±3.64 | 5.97±1.33 | 12.46±2.33 | 9.24±2.27 |
| FSH(mIu\ml) | 5.48±1.54 | 5.34±0.69 | 5.38±1.03 | 6.22±0.618 |
| LH\FSH ratio | 2.36±0.26 | 1.133±0.3 | 2.34±0.35 | 1.49±0.38 |
| TG (mg\dl) | 183±15.9 | 109.5±32.77 | 119.33±28.25 | 105.6±18.99 |
| Cholesterol (mg\dl) | 188.33±11.33 | 127.6±47.19 | 177.92±8.57 | 143.9±35.99 |
| LDL (mg\dl) | 141.08±22.83 | 108.5±19.06 | 115.58±10.15 | 111.4±10.15 |
| HDL( mg\dl) | 43.67±7.06 | 49.8±4.41 | 47.58±5.05 | 48±17.64 |
| BMI (kg\m²) | 32.43±3.14 | 31.254±0.71 | 23.19±1.28 | 23.45±0.63 |
| Waist circumference (cm) | 93.58±4.66 | 91.3±4.27 | 77.92±6.93 | 72.9±3.84 |

They were recruited from outpatient clinic of Endocrinology and Metabolism, Ain Shams University Hospital.

All subjects were submitted to the following:

**1.** Full medical history taking and clinical examination

**2.** Anthropometric measurements including:

Weight, height, Body mass index (weight in kilograms divided by height in meters squared),waist circumference.

**3. Laboratory measurements including:**

- Fasting plasma insulin by Enzyme Amplified Sensitivity Immunoassay (EASIA) performed on micro titerplates. Normal range of fasting insulin is 3-22 uIU/ml.
- Fasting plasma glucose
- Estimation of insulin resistance by HOMA measurement.
- Lipid profile (cholesterol, triglycerides, LDL-C, HDL), by enzyme colorimetric assay using commercially available Kit (Boehringer Mannheim, Germany) after an overnight 12 hours fasting. Normal range for serum

cholesterol up to 200 mg/dl (11), and for serum triglycerides: up to 200 mg/dl.(12) , estimation of serum HDL was done by precipitation with dextran sulphate Ciba Corning Diagnostics, Frenwald, Germany. Normal range: 30-60mg/dl in males and 40-70mg/dl in females. **(13) ,** LDL-C was calculated according to the Fridwald formula (14) as follows: LDLc= Total cholesterol-TG/5-HDLc.

- Fasting plasma visfatin concentration by using the RayBiotech, Inc. Visfatin Enzyme immunoassay (EIA) Kit is an in vitro quantitative assay for detecting visfatin peptide based on the principle of competitive Enzyme immunoassay . Normal range 20-30ng\ml.

- LH/FSH ratio

**4- Pelvic ultrasound scans for all the cases.**

**Criteria considered for selection of PCOS cases:**

- Menstrual irregularities, clinical evidence of hyper-androgenism, high LH/FSH ratio, Ovarian cysts by pelvic u/s.

**Exclusion Criteria:**

- Age over 40 years, Morbid obesity (BMI>40Kg/m2), Known cardiovascular disease, Thyroid disease, hyper-prolactinemia, hyper-cortisolemia, neoplasm, DM, hypertension,(blood pressure>140/90 mmHg), Renal and liver diseases, History of intake of any drug during the last 6 months that may affect the insulin sensitivity or hormonal profile such as : oral contraceptives, glucocorticoids, ovulation induction agents, anti diabetic and anti obesity drugs, estrogenic, antiandrogenic or anti hypertensive medication.

- **Statistical Analysis** :data collected ,verified, revised then analyzed statistically using SPSS statistical package for special science version 12 (SPSS Inc., Chicago, IL, USA).

Data were expressed as mean ± standard deviation.

Unpaired (student') t test was used for independent samples. A one-way ANOVA with post hoc tests was used to determine LSD (least significant difference) , Linear regression analysis, spearman's correlation coefficient denoted symbolically ***r***, was used to study correlation between different studied variables , level of Significance (P) was expressed as follow:

**P value (**>0.05 is non-significant (N.S)
**P value**<0.05 is significant (Sig)
**P value** <0.001 is highly significant (H.S)

And in order to select visfatin cutoff value that best combined sensitivity and specificity, **Receiver-operator characteristic (ROC**) curves were calculated the area under the curve (AUC) and 95% confidence interval (CI) were calculated for each plot.

**Sensitivity:** the ability of the test to detect those who are truly diseased (true positive rate)

**Specificity** is the ability of the test to detect those who are free of disease (true negative rate)

**PPV:** positive predictive value is th2 proportion of patients with an outcome or disease if the test is positive, is the percentage of true positive to all positive by the examined test

**NPV** negative predictive value is the proportion of free cases in negative results

## Results

**The descriptive data for the studied 4 subgroups are shown in (table1)**

**Comparing** the **Lean PCO group** with the **Lean control group, it was found, a** highly statistically significant difference (P≤0.001) regarding: LH. also a statistical significant difference (P≤ 0.05) regarding: visfatin ,fasting plasma insulin ,HOMA-IR ,FSH, cholesterol , Waist circumference and an insignificant statistical difference (P>0.05) as regard : FPG , LH\FSH ratio , TG , LDL , HDL & BMI . (table 2)

**Table (2):** Comparison between obese PCO and obese control

| | Obese PCO | Obese control | T | P | Sig. |
|---|---|---|---|---|---|
| | mean±SD | mean±SD | | | |
| Visfatin(ng) | 79.25±6.85 | 58.8±8.22 | 2.100922 | <0.05 | S |
| FPG(mg\dl) | 91.75±6.79 | 78.3±7.78 | 4.270776 | <0.001 | HS |
| Fasting plasma insulin(IU\ml) | 13.33±3.47 | 9.1±3.54 | 2.816286 | <0.05 | S |
| HOMA -IR | 3.00±0.72 | 1.592±0.53 | 5.249139 | <0.05 | S |
| LH(mIu\ml) | 12.83±3.64 | 5.97±1.33 | 6.043518 | >0.05 | NS |
| FSH(mIu\ml) | 5.48±1.54 | 5.34±0.69 | -12.8208 | >0.05 | NS |
| LH\FSH ratio | 2.36±0.26 | 1.133±0.3 | 9.916423 | >0.05 | NS |
| TG (mg\dl) | 183±15.9 | 109.5±32.77 | 6.484364 | >0.05 | NS |
| Cholesterol (mg\dl) | 188.33±11.33 | 127.6±47.19 | 3.974645 | <0.001 | HS |
| LDL (mg\dl) | 141.08±22.83 | 108.5±19.06 | 3.647827 | <0.001 | HS |
| HDL( mg\dl) | 43.67±7.06 | 49.8±4.41 | -1.09751 | >0.05 | NS |
| BMI (kg\m²) | 32.43±3.14 | 31.254±0.71 | 9.654881 | <0.05 | S |
| Waist circumference (cm) | 93.58±4.66 | 91.3±4.27 | 11.40892 | >0.05 | NS |

**The obese PCO group** with the **obese control group**, a highly statistically significant difference (P≤0.001) as regards: FPG, cholesterol, LDL. Also a statistically significant difference (P≤ 0.05) regarding Visfatin, HOMA-IR, fasting plasma insulin, BMI And insignificant difference (P>0.05) regarding LH, FSH ,LH\FSH ratio & TG & HDL & waist circumference. (Table 3).

**Table (3):** Comparison between lean PCO and lean control

| | Lean PCO | Lean control | t | P | Sig. |
|---|---|---|---|---|---|
| | mean±SD | mean±SD | | | |
| Visfatin(ng) | 86.08±6.35 | 59.7±12.42 | 2.160369 | <0.05 | S |
| FPG(mg\dl) | 89.58±4.98 | 85.9±9.45 | 1.11114 | >0.05 | NS |
| Fasting plasma insulin(IU\ml) | 14.92±3.55 | 8±1.63 | 6.022317 | <0.05 | S |
| HOMA-IR | 3.31±0.69 | 1.662±0.22 | 7.811482 | <0.05 | S |
| LH(mIu\ml) | 12.46±2.33 | 9.24±2.27 | 3.287041 | <0.001 | HS |
| FSH(mIu\ml) | 5.38±1.03 | 6.22±0.618 | -2.36704 | <0.05 | S |
| LH\FSH ratio | 2.34±0.35 | 1.49±0.38 | 5.416709 | >0.05 | NS |
| TG (mg\dl) | 119.33±28.25 | 105.6±18.99 | 1.624889 | >0.05 | NS |
| Cholesterol (mg\dl) | 177.92±8.57 | 143.9±35.99 | 2.920434 | <0.05 | S |
| LDL (mg\dl) | 115.58±10.15 | 111.4±10.15 | 0.663825 | >0.05 | NS |
| HDL( mg\dl) | 47.58±5.05 | 48±17.64 | -0.16986 | >0.05 | NS |
| BMI (kg\m²) | 23.19±1.28 | 23.45±0.63 | -0.63011 | >0.05 | NS |
| Waist circumference (cm) | 77.92±6.93 | 72.9±3.84 | 2.142308 | <0.05 | S |

On comparing the **Lean PCO group** with the **obese control group**,

A highly statistically significant difference (P≤0.001) as regards: FPG and , fasting plasma insulin, cholesterol, LDL , a statistically significant difference (P≤ 0.05) was found regarding visfatin, HOMA-IR ,HDL, BMI and an insignificant statistical difference (P>0.05)as regards: LH, FSH, LH\FSH ratio, TG, waist circumference (table 4).

**Table (4) :** Comparison between lean PCO and obese control regarding clinical laboratory parameters

| | Lean PCO | Obese control | t | P | Sig. |
|---|---|---|---|---|---|
| | mean±SD | mean±SD | | | |
| Visfatin(ng) | 86.08±6.35 | 57.9 ±8.22 | 2.109816 | <0.05 | S |
| FPG(mg\dl) | 89.58±4.98 | 78.3±7.78 | 3.955942 | <0.001 | HS |
| Fasting plasma insulin(IU\ml) | 14.92±3.55 | 9.1±3.54 | 3.829703 | <0.001 | HS |
| HOMA-IR | 3.31±0.69 | 1.59±0.53 | 6.59906 | < 0.05 | S |
| LH(mIu\ml) | 12.46±2.33 | 5.97±1.33 | 8.155204 | >0.05 | NS |
| FSH(mIu\ml) | 5.38±1.03 | 5.34±0.69 | 0.094455 | >0.05 | NS |
| LH\FSH ratio | 2.34±0.35 | 1.133±0.3 | 8.62758 | >0.05 | NS |
| TG (mg\dl) | 119.33±28.25 | 109.5±32.77 | 0.745622 | >0.05 | NS |
| Cholesterol (mg\dl) | 177.92±8.57 | 127.6±47.19 | 3.32567 | <0.001 | HS |
| LDL (mg\dl) | 115.58±10.15 | 108.5±19.06 | 3.647827 | <0.001 | HS |
| HDL( mg\dl) | 47.58±5.05 | 49.8±4.41 | -2.48175 | <0.05 | S |
| BMI (kg\m²) | 23.19±1.28 | 31.254±0.71 | 1.257317 | <0.05 | S |
| Waist circumference (cm) | 77.92±6.93 | 91.3±4.27 | 1.197893 | >0.05 | NS |

On comparing the **obese PCO group** with the **lean PCO group**,

A highly statistically significant difference (P≤0.001) regarding : LDL, statistically significant difference (P≤ 0.05) regarding : visfatin, fasting plasma insulin , HOMA-IR (figure 1),cholesterol, BMI (table 5)and insignificant statistical difference (P>0.05)as regards: FPG, LH, FSH, LH\FSH ratio TG ,HDL ,waist circumference.

**Table (5):** Comparison between obese PCO and lean PCO regarding clinical & laboratory parameters

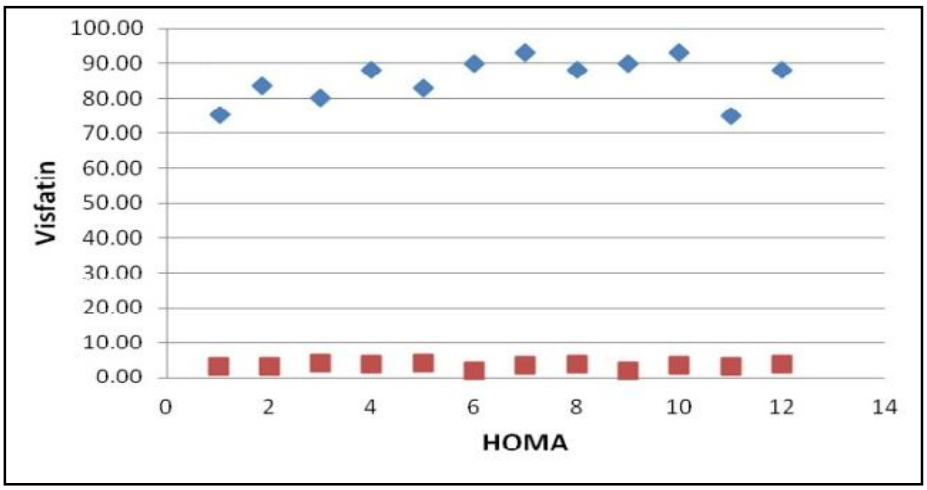
| | Obese PCOS mean±SD | Lean PCOS mean±SD | T | P | Sig. |
|---|---|---|---|---|---|
| Visfatin(ng) | 79.25±6.85 | 86.08±6.35 | 2.073873 | <0.05 | S |
| FPG(mg\dl) | 91.75±6.79 | 89.58±4.98 | 2.1 | >0.05 | NS |
| Fasting plasma insulin(IU\ml) | 13.33±3.47 | 14.92±3.55 | 2.07 | <0.05 | S |
| HOMA - IR | 3.00±0.72 | 3.31±0.69 | 0.29 | <0.05 | S |
| LH(mIu\ml) | 12.83±3.64 | 12.46±2.33 | 2.09 | >0.05 | NS |
| FSH(mIu\ml) | 5.48±1.54 | 5.38±1.03 | 2.09 | >0.05 | NS |
| LH\FSH ratio | 2.36±0.26 | 2.34±0.35 | 2.07 | >0.05 | NS |
| TG (mg\dl) | 183±15.9 | 119.33±28.25 | 2.1 | >0.05 | NS |
| Cholesterol (mg\dl) | 188.33±11.33 | 177.92±8.57 | 2.08 | <0.05 | S |
| LDL (mg\dl) | 141.08±22.83 | 115.58±10.15 | 2.13 | <0.001 | HS |
| HDL( mg\dl) | 43.67±7.06 | 47.58±5.05 | 2.08 | >0.05 | NS |
| BMI (kg\m²) | 32.43±3.14 | 23.19±1.28 | 2.13 | <0.05 | S |
| Waist circumference (cm) | 93.58±4.66 | 77.92±6.93 | 2.09 | >0.05 | NS |

**As regards the correlation between the serum visfatin and the different parameters in lean PCO patients**, there was a highly statistically significant positive correlation (P≤0.001) between visfatin and Wt (r=0.020917) and statistical significant positive correlation (P≤0.05) between visfatin and cholesterol (r=0.130610) , while there was a statistical significant negative correlation with Age (r=-0.20096) and a highly statistically significant negative correlation (P≤0.001) between visfatin and FPG (r=-0.32022).(table 6), also non significant correlation with HOMA (figure 1) and non significant positive correlation with LH&FSH (figure 2)

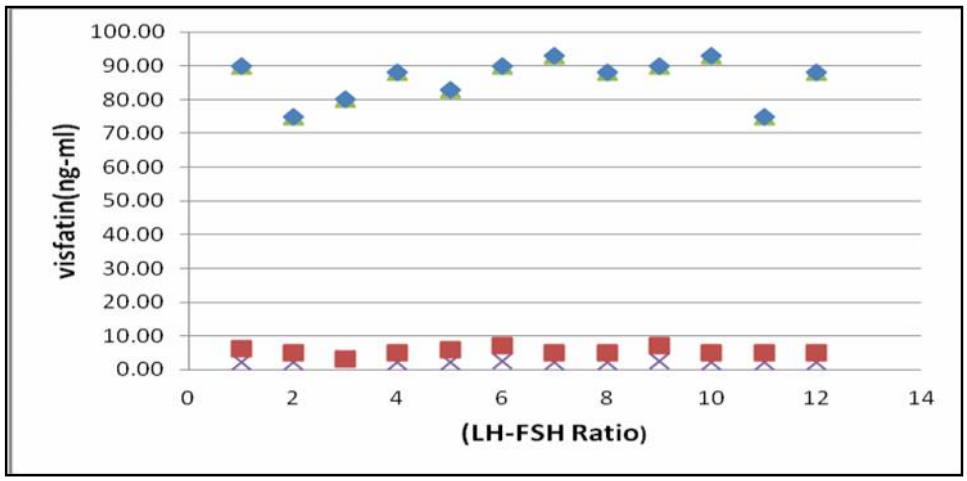
**Table (6):**correlation between visfatin and other measured parameters in lean PCOS

| Cases (lean) | | |
|---|---|---|
| | **Visfatin(ng/ml)** | |
| | ***R*** | ***P*** |
| Age(yrs) | -0.20096 | <0.05 (*) |
| Fasting plasma glucose(mg/dl) | -0.32022 | <0.001 (**) |
| Fasting plasma insulin(IU\ml) | -0.16458 | >0.05 |
| HOMA-IR | -0.33711 | >0.05 |
| LH(mIU\ml) | -0.83093 | >0.05 |
| FSH(miU\ml) | -0.78535 | >0.05 |
| LH-FSH Ratio | 0.041297 | >0.05 |
| TG(mg\dl) | -0.14115 | >0.05 |
| cholesterol(mg\dl) | 0.130610 | <0.05 (*) |
| LDL(mg\dl) | -0.26937 | >0.05 |
| HDL(mg\dl) | 0.500495 | >0.05 |
| Wt (kg) | 0.020917 | <0.001 (**) |
| Ht (m) | 0.121693 | >0.05 |
| BMI(kg\m$^2$) | 0.09231 | >0.05 |
| Waist circumference(cm) | -0.84825 | >0.05 |

**Figure (1):** Scatter diagram showing the relation between Visfatin and HOMA among lean cases, there was a non significant negative correlation between Visfatin and HOMA P>0.05



**Figure(2):** Scatter diagram showing the relation between Visfatin and (LH-FSH) among lean cases, there was a non significant positive correlation between Visfatin and (LH-FSH) P>0.05




**As regards the correlation between the serum visfatin and the different parameters in obese PCO patients**, there was a highly statistically significant positive correlation (P≤0.001) between visfatin and LH\FSH ratio (r=0.0125)(figure 3), HOMA (r=0.075)(figure 4) , also there was a statistical significant positive correlation (P≤0.05) between visfatin and fasting plasma insulin (r=0.149) LH (r=0.508), FSH (r=0.47), TG(r=0.141) and Waist circumference (r=0.16), BMI (r=0.741), while there was a statistical significant negative correlation with LDL(r=-0.05), HDL(r=-0.29) and Ht(r=-0.32). (table 7) .

After blotting ROC curve to define the best cutoff to visfatin (ng/ml)to detect PCOS it was found that Visfatin (ng/ml) was reliable to predict PCO P<0.0001 and AUC (area under the curve) is 87.5%, and the best cut off value was 83 with a sensitivity of 100%, specificity 80%, PPV 50% and NPV 100% with a diagnostic accuracy of 83.3%. (figure 5)

**Table (7):** Correlations between visfatin and other measured parameters in obese PCO

| Cases (Obese) | | |
|---|---|---|
| | **Visfatin(ng/ml)** | |
| | ***R*** | ***p*** |
| Age(yrs) | -0.15 | >0.05 |
| Fasting plasma glucose(mg\dl) | 0.347 | >0.05 |
| Fasting plasma insulin(IU\ml) | 0.149 | <0.05(*) |
| HOMA - IR | 0.075 | <0.001(**) |
| LH(mIU\ml) | 0.508 | <0.001(*) |
| FSH(miU\ml) | 0.47 | <0.05(*) |
| LH-FSH Ratio | 0.0125 | <0.001(**) |
| TG(mg\dl) | 0.141 | <0.05(*) |
| cholesterol(mg\dl) | -0.174 | >0.05 |
| LDL(mg\dl) | -0.05 | <0.05(*) |
| HDL(mg\dl) | -0.29 | <0.05(*) |
| Wt (kg) | -0.23 | >0.05 |
| Ht (m) | -0.32 | <0.05(*) |
| BMI(kg\m²) | 0.741 | <0.05(*) |
| Waist circumference(cm) | **0.16** | <0.05(*) |

**Figure (3):** Scatter diagram showing the relation between Visfatin and Ratio LH-FSH among obese Cases, There was a highly significant positive correlation between Visfatin and LH-FSH P<0.001.

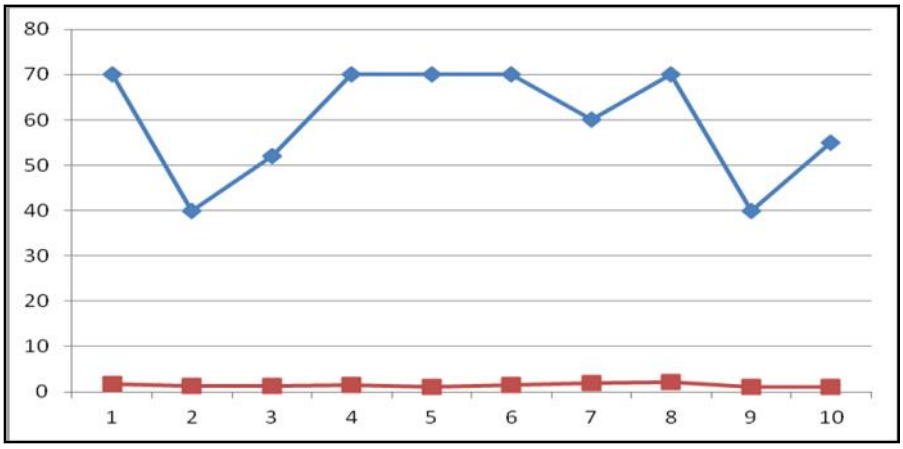



**Figure (4):** Scatter diagram showing the relation between Visfatin and HOMA among obese Cases, there was a highly significant positive correlation between Visfatin and HOMA P<0.001.

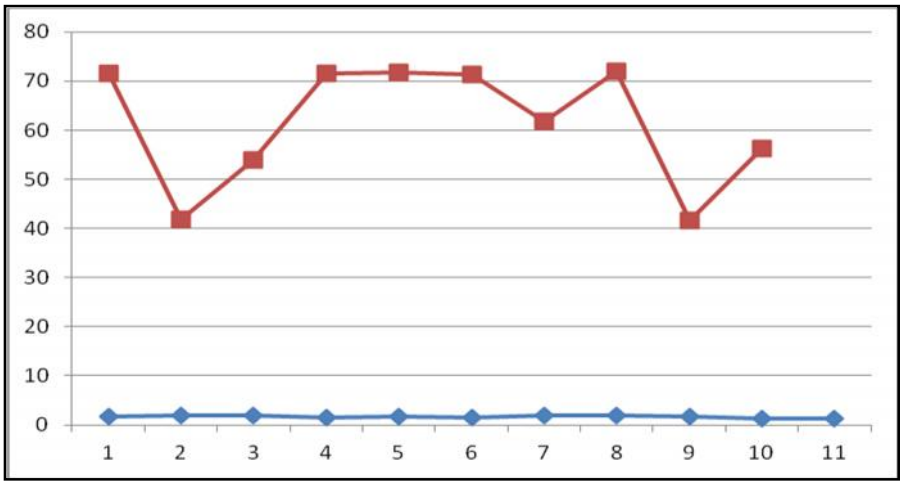
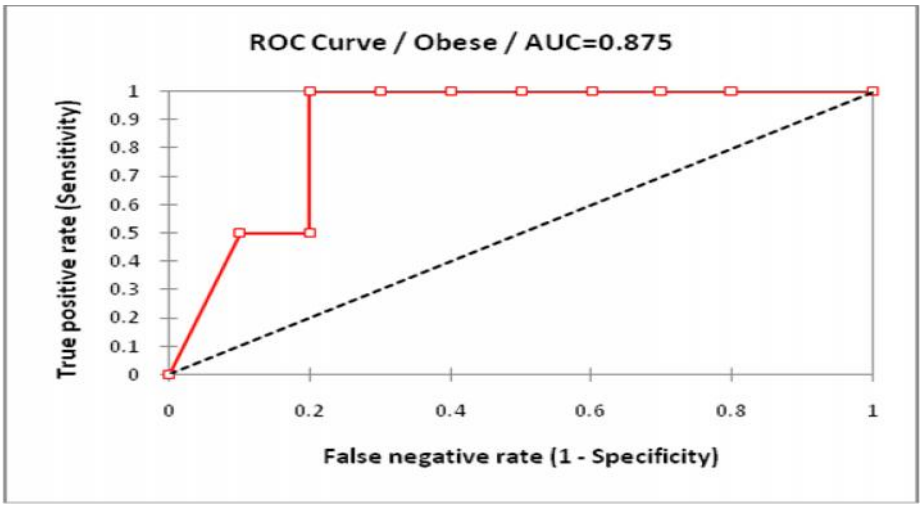



**Figure (5):** Receiver Operating Characteristic (ROC) curve to define the best cutoff to Visfatin (ng/ml) to detect PCO

| | AUC | st error | P | 95%CI |
|---|---|---|---|---|
| Visfatin (ng/ml) | 0.875 | 0.032 | **<0.0001** | 0.812- 0.938 |

Visfatin (ng/ml) was reliable to predict PCO P<0.0001 and AUC (area under the curve) is 87.5%. and the best cut off value was 83 with a sensitivity of 100%, specificity 80%, PPV 50% and NPV 100% with a diagnostic accuracy of 83.3%



## Discussion

PCO is characterized by chronic anovulation, hyper-gonadism, central obesity, and insulin resistance (14) Recently, it has been shown that visceral adipose tissue produces visfatin, which may regulate insulin sensitivity (6).It exhibits insulin like activity and has been shown to activate the insulin receptor in various insulin sensitive cell types in vitro , stimulate glucose uptake into adipocytes and muscle cells, and suppress glucose release from hepatocytes in vitro (6).In the present study we found that visfatin is significantly higher in lean PCOS compared to obese PCOS cases, obese and lean contol , however obese PCOS are significantly higher than obese control and these results came in agreement with Pagano et al.,(15) who found higher visfatin level in lean PCOS cases compared to obese PCOS cases ., and Ozkaya et al., (16) who reported high serum visfatin level in lean PCOS women ,as well as Ramazan et al.,(17) which showed high plasma visfatin level in lean women with PCOS than healthy women and Tan et al.,(18)who found increased visfatin in obese and overweight women with PCOS compared to BMI-matched controls.

On the other hand, other studies(19) reported increased visfatin conc in PCOS women with no significant differences between obese and non obese . and others who reported increased adipose tissue visfatin expression and plasma visfatin in obese PCOS compared to lean subjects(18). so from the previous finding they suggested that visfatin could play a role in pathogenesis of PCOS (18), this controversy might be attributed to the fact that visfatin levels were various and varied 2-10 times compared between the studies as well as it seemed to be an ethnic difference as it was found to be higher in Asian women with PCOS than Caucasian women (20).

In the present study fasting plasma glucose was found to be significantly higher in PCO cases (obese & lean) compared to their control more in obese PCOS, however; the difference between obese and lean PCOS did not reach a statistical significant value, and this agreed with several studies which assessed glucose tolerance among PCOS women and risk of developing T2DM which was found to be increases 3-7 times (21-22). So guidelines from the Androgen excess Society recommend that a 2-hour OGTT must be performed on all obese women with PCOS**(23).**

Enforcing the previous results we found a sig higher fasting plasma insulin level and HOMA-IR in PCO cases whether obese or lean compared to their control, more in obese PCOS with significant difference compared to lean PCOS.

As regard fasting insulin previous finding came inconsistent with studies which found that Insulin resistance with resultant hyperinsulinaemia is a prominent feature of PCOS, weather obese or normal weight**(24-25),** moreover, obese women develop a greater degree of Insulin resistance as their body mass increases(**26)**.

As regard HOMA-IR our results goes close to the study found that abdominal obesity is thought to induce insulin resistance by expressing and secreting several peptide hormones and cytokines e.g tumor necrosis α (TNF α) which is high in obese PCOS (**27) and others** (28)who found the prevelance of insulin resistance to be 77% of PCOS patients and those who found insulin resistance to be 64%(Catherine et al.,2005)(28), claiming this difference to the ethnic difference in the group and the lack of well accepted criteria for diagnosis of PCOS, however this disagree with **Marsden et al.(30)**who documented impaired tissue insulin sensitivity in obese PCOS as well as in lean PCOS women and showed that the impaired insulin sensitivity appears to be independent of obesity.

In our study we found significant higher waist circumference in lean PCO cases in comparison to lean normal control , this result came in agreement with ***Mauriege et al.(31)***who found that in these lean PCO subjects , the noradrenaline resistance in the subcutaneous adipose tissue is due to two major defects in the lipolytic cascade, both these defects could promote the accumulation of fat in the subcutaneous and abdominal depot, although these subjects were lean they had slightly larger fat cell size compared to controls, likewise others who (**32)** found that majority of PCOS pt have android obesity even in lean.

As regard serum visfatin , we find a significant negative correlation with FPG in lean PCO cases (r= -0.32022) but insignificant correlation among obese PCO(r=0.347) , this agree with ***Chen et al(9)***who found negative correlation between visfatin level and plasma concentration of glucose**,** and B**erndt et al**.,(33)who found no correlation between them in obese PCOS.

Furthermore, as regard correlation of visfatin and parameters of insulin sensitivity (fasting insulin – HOMA-IR), in obese PCOS there is highly significant

positive correlation between visfatin and HOMA-IR (r=0.075) and significant correlation with fasting plasma insulin (r=0.149)but in lean PCOS we found non sig negative correlation between visfatin and both HOMA-IR (r= -0.33711) and fasting insulin level (r=-0.16458) and these results goes with several studies who supported this correlation (19)(34-35) and others who clarified evidence of association between insulin resistance and subclinical inflammation involving cytokines derived from adipose tissue as a major regulator of insulin resistance (36) athough this correlation denied in other studies (15)(37)

Additionally, we found a highly sig positive correlation between visfatin and body weight and significant positive correlation with BMI in lean PCOS and this agreed with chan et al., and Berndt et al(33)(38). However , disagree with Haider et al., and Krzyzanowska et al.(39)(8), who found no association between visfatin and BMI

Furthermore we found , significant positive correlation between visfatin and waist circumference in obese PCOS(r=0.16) this consistent with Manal et al., and Sandeep et al.,(34)(37) who found positive correlation between visfatin and waist circumference in PCO and disagree with Haider et al (39)who found this correlation in male but not in female .

As regard lipid profile , we found in obese PCOS there is high significant elevation of LDL (P<0.001)with significant elevation of T.cholesterol (P<05) and non significant elevation of TG (P>0.05) and non significant decrease in HDL(P>0.05) compared to lean PCOS and control groups and this agreed with studies (40-41) who found that in the presence of hyperandrogenism and hyperinsulinemia, an atherogenic lipid profile is present in PCO women. Furthermore lipid profile in women with PCOS is characterized by elevated TG, LDL, and reduced HDL levels and these abnormal lipid profile tend to increase the risk of developing cardiovascular disease and metabolic syndrome in women with PCOS.

However our results came in contrast to studies which reveals who found that there is no difference in lipid profile among lean or obese PCOS patients(42).

Moreover, we observed in lean PCOS visfatin showed significant positive correlation with T. cholesterol and non significant negative correlation with LDL &TG and non significant positive correlation with HDL. But in obese PCOS visfatin showed significant positive correlation with TG, significant negative correlation with LDL, HDL and non significant negative correlation with T.cholesterol. This agreed with **Ching et al.(43)**, reported that serum visfatin positively correlated with serum cholesterol in lean PCOS and Jin et al who recorded serum visfatin level to be negatively correlated with HDL-C in obese subjects **Jin et al., (44)**.

In our study LH/FSH ratio was found to be higher in PCOS cases more in obese compared to lean PCOS and their controls however this difference was statistically insignificant but agreed with ***Kandasamy et al*..(22)**

Also we found statistically significant positive correlation between visfatin and FSH(r=0.47) , LH( r=0.508) in obese PCOS and non significant negative correlation in lean PCO, this agreed with studies (19)(45) who demonstrated that visfatin is positively correlated with LH levels in obese PCOS patients and this positive correlation to LH levels further reflects a putative involvement of this specific adipocytokine in the hypothalamic-pituitary-ovarian axis pathology observed in PCOS this disagree with others (34) who reported that S.visfatin positively correlated with FSH &negatively correlated with LH.

In the present work we found negative correlation between serum visfatin and age in both obese and lean PCOS being insignificant(r=-0.15)with obese PCOS this goes with ***Jin et al. (44)***found significant negative association between fasting serum visfatin and age in an obese adolescent population independent of gender and BMI.

This might be explained by interplay of certain hormones which abnormally fluctuate with age in obese adolescents, such as androgen, estrogen, growth hormone, etc., which may influence the secretion of visfatin.

## Conclusion

We concluded that visfatin and insulin resistance are higher in lean PCOS patients compared to obese PCOS cases..

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