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Research Article

Visfatin Serum Levels in PCO Patients Vs Normal Female Subjects

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2. Keywords

Adipocytokine; Polycystic ovary syndrome; Nicotinamidephosphoribosyltransferase; Visfatin

1. Abstract

1.1. Aim: The goal of the current research is to put in comparison the serum levels of visfatin between cases with PCOS and normal female subjects and to evaluate the linkage between serum visfatin levels and different obtained study subject parameters.

1.2. Methodology: This case-control research study enrolled 74 subjects with polycystic ovarian syndrome and 74 subjects that are age and body mass index matched subjects as controls. Serum levels of visfatin are measured by the enzyme-linked immunosorbent assay lab technique. Cases with polycystic ovarian syndrome are categorized into 2 subdivisions relying on the existence of clinical or biochemical evidence of hyperandrogenism. The statistical difference in visfatin serum levels between the hyperandrogenic category of subjects and non-hyperandrogenic research study category are additionally evaluated. The research study was conducted at private hospital in Jeddah, KSA, United Doctors Hospital, over 2 years from July 2015 to July 2017.

1.3. Results: Visfatin serum levels in cases with PCOS have been similar to the research control group. On the other hand, cases that were hyperandrogenic had statistically significantly greater mean value of visfatin serum levels much more than cases that are non-hyperandrogenic (3.87 ng/mL; 95% Confidence Intervals [CIs], 3.09-4.85 in hyperandrogenic research group *vs.* 2.69 ng/mL; 95% CIs, 2.06-3.52 in non-hyperandrogenic research group; P=0.038). In female subjects with polycystic syndrome, visfatin serum levels showed positive statistical correlation with body mass index (r=0.23; P=0.047) and the log free androgenic index (r=0.27; P=0.021) and statistically correlated in a negative fashion with serum high-density lipoprotein serum levels of cholesterol (r=−0.37; P=0.025). Apart from serum HDL cholesterol levels, those statistically observed correlations were additionally displayed in control subjects.

1.4. Conclusion: Serum levels of visfatin in cases with polycystic ovarian syndrome were similar to those in the research control group. On the other hand hyperandrogenic subjects displayed statistically significant greater visfatin serum levels in comparison to non-hyperandrogenic subjects, and serum visfatin have a positive direct correlation with free androgenic index in both polycystic ovarian syndrome subjects and research control subjects.

3. Introduction

Polycystic ovary syndrome is clinically featured and described as a condition of chronic anovulatory and hyperandrogenic disorder is considered a wide spread endocrinal disease in females in reproductive phase of life. Insulin resistance is a cornerstone pathophysiological feature of this disease. As a consequence, in addition to its correlation with morbid reproductive issues, polycystic ovarian syndrome is also clinically expressed as a metabolic disease. Females having polycystic ovarian syndrome show greater liability to hypertensive disorders and dyslipidemia and have raised risk of type 2 DM and subclinical atherosclerotic changes. Obesity a famous epidemic is a prominent feature in cases suffering poly cystic ovarian disease is frequently featured in

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those type of patients reaching around 20%-70% [1,2].

Visfatin is a recently discovered adipokine existing in various tissues e.g. subcutaneous, visceral, perivascular, and epicardial fatty tissues. Visfatin serum levels are in strong correlation with body mass index or body fat percentage and are greater in obese cases than that observed in normal weight range control subjects .In the beginning, visfatin was believed to chiefly comprise insulin-mimetic biochemical features e.g. triggering glucose uptake in adipocyte cells and inhibiting release of glucose from liver cells in vitro .Conversely, successive research studies performed have displayed correlation between visfatin and inflammatory pathophysiological pathways , dysfunction of endothelial system and atherosclerotic process; these observed correlations imply a likely value of serum visfatin as a biological marker for low-grade inflammatory processes and metabolic issues helping in clinical practice diagnosis of these conditions .A prior research group. ,uncovered the fact that visfatin is not only secreted by fat cells but in addition by cells responsible for inflammation e.g. macrophages in subcutaneous tissue , implying that visfatin could be used as aproinflammatory biological marker [3-5]. Poly cystic ovarian disease is correlated with the abnormal secretory activity in the form of producing adipokines, triggering and provoking inflammatory process and insulin resistance. considerable research studies mentioned that expressive genetic activity or visfatin serum levels are in a statistically significant manner greater in females with polycystic ovarian disease in comparison to those matched research control subjects .A prior research group performed a study and mentioned, that serum visfatin level is considered as a predictor biological tool for dysfunction of endothelial system in females having polycystic ovarian disease. On the other hand, several research studies previously performed mentioned that there was no observed statistical differences in visfatin serum levels among cases of polycystic ovarian disease and matched research controls [6-8].

The aim of the present research study performed by our group is to compare and contrast between visfatin serum levels in females having polycystic ovarian disease to females devoid of polycystic ovarian disease features and in addition to evaluate the statistically observed correlations between serum visfatin levels and different observed research parameters. Taking into account that elevated serum levels of visfatin have been observed in polycystic ovarian disease cases with hirsutism and that positive statistical correlations between levels of serum visfatin and serum androgen levels are observed in various research subjects, this current research performed additionally evaluated if visfatin serum levels varied among hyper androgenic and norm androgenic cases with polycystic ovarian disease. To diminish the impact of obesity, the research approach was conducted in non-obese females suffering from polycystic ovarian disease with age- and BMI-matched research controls [9-11].

4. Methodology

This is a cohort research study performed over 2 years from July 2015 till July 2017, a total of 74 females premenopausal have been recruited as poly cystic ovarian disease, and a diagnosis relied on the 2003 Rotterdam guidelines the cases have been matched. The research study was conducted at a private hospital united doctors hospital KSA. With cases based on age (±3 year) and body mass index (±1 kg/m2). Clinical data e.g. body weight, height, waist circumference and blood pressure (BP) were evaluated, and BMI was obtained. All cases recruited for the research study were assessed for serum LH, FSH and E2, total testosterone, free testosterone , 17-OH progesterone and sex hormone binding globulin by using radioimmunoassay Serum cholesterol, triglyceride , high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and hemoglobin A1c serum levels were also assessed in addition to fasting insulin and OGTT in females with polycystic ovarian disease. In the controls, serum total T, free T, SHBG, fasting glucose and insulin, hemoglobin A1c, total cholesterol, TG, HDL cholesterol and LDL cholesterol levels were evaluated. Serum visfatin was evaluated by human visfatin enzyme-linked immunosorbent assay, and the intra- and inter-assay coefficients of variation were <10% and <8%, respectively.

5. Statistical Analysis

Hormonal and other metabolic parameters were compared using a Student's t-test. To assess the correlations between serum visfatin levels and each parameter, Pearson's correlation analysis was used. All data analyses were performed using the Statistical Package for the Social Sciences software (version 22.0; IBM SPSS, Armonk, NY, USA), and statistical significance was accepted for 2-sided P-values <0.05.

5.1. Results: The clinical and endocrine characteristics are shown in **Table 1**. By definition, there were significant differences in the hirsutism score and serum androgen levels between women with PCOS and the controls. There were also significant differences in systolic and diastolic BP, fasting glucose, fasting insulin, HOMA-IR, and uric acid levels between the 2 groups. However, serum lipid, hemoglobin A1C, and visfatin levels were similar between the 2 groups. For further analysis, women with PCOS were divided into 2 subgroups based on the presence of hyperandrogenism.

Table 1: Clinical and biochemical parameters of females that are not obese with polycystic ovary disease matched control research subjects. Data are shown as the means ± standard deviation, median (interquartile range), or geometric mean (95% confidence intervals). *P*-values are indicated for the differences between groups, as analyzed using a Student's *t*-test.
PCOS, polycystic ovary syndrome; BMI, body mass index; WC, waist circumference; BP, blood pressure; SHBG, sex hormone binding globulin; FAI, free androgen index; HOMA-IR, homeostasis model assessment of insulin resistance; OGTT, oral glucose tolerance test; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Parameters of study subjects	Control matched research subjects (n=74)	p-value
Anthropometric data		
Age (years)	24.4+/-5.0	0.461
BMI(Kg/m^2)	20.4+/-2.1	0.95
Waist Circumference(cm)	75.5+/-6.6	0.256
Hirsutism Clinical Score	0(0-3)	<0.001
Systolic blood pressure measurement (mmHg)	105.7+/-9.9	<0.001
Diastolic blood pressure measurement(mmHg)	64.3+/-6.3	<0.001
Hormonal variables		
Total testosterone (ng/ml)	0.22(0.18-0.29)	<0.001
Free testosterone(pg/ml)	0.36(0.27-0.47)	<0.001
SHBG(nmol/L)	54.9(44.8-67.2)	0.401
FAI	1.4(1.1-1.7)	<0.001
Lutenizing hormone (IU/L)	Not available	_
Follicle stimulating hormone(IU/L)	Not available	_
Estradiol(pg/ml)	Not available	_
Metabolic variables		
Fasting blood glucose level (mg/dl)	84.9+/-6.1	0.04
Fasting insulin level	5.37(4.33-6.66)	<0.001
HOMA-IR	1.20(0.98-1.47)	0.002
75 gm OGTT glucose level	Not available	_
75 gm OGTT Insulin level	Not available	_
Total cholesterol level (mg/dl)	172.0+/-26.6	0.521
Triglyceride level(mg/dl)	75.1+/-27.4	0.307
HDL cholesterol level (mg/dl)	62.14+/-10.7	0.202
LDL cholesterol level (mg/dl)	94.9+/-21.9	0.943
HaemoglobinA1C (%)	5.50+/-0.23	0.339
Serum Uric acid(mg/dl)	4.25+/-0.69	0.031
Serum vesfatin level (ng/ml)	3.28+/-1.01	0.789

By definition, there were significant differences in the hirsutism score and serum androgen levels between women with PCOS and the controls. There were also significant differences in systolic and diastolic BP, fasting glucose, fasting insulin, HOMA-IR, and uric acid levels between the 2 groups. However, serum lipid, hemoglobin A1C, and visfatin levels were similar between the 2 groups. For further analysis, women with PCOS were divided into 2 subgroups based on the presence of hyperandrogenism. If a patient has any of the clinical hyperandrogenism or biochemical hyperandrogenemia, then she was categorized as the hyper androgenic group. Differences in serum visfatin levels between the hyper androgenic and non-hyperandrogenic groups were assessed **(Table 2)**.

Table 2: Clinical characteristics and biochemical parameters of non-obese polycystic ovary disease cases with and without features of clinical hyper androgenism data are shown as the means ± standard deviation, median (interquartile range), or geometric mean (95% confidence intervals). P-values are indicated for the differences between groups, as analyzed using a Student's *t*-test.
PCOS, polycystic ovary syndrome; BMI, body mass index; WC, waist circumference; BP, blood pressure; HOMA-IR, homeostasis model assess¬ment of insulin resistance; OGTT, oral glucose tolerance test; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SHBG, sex hormone binding globulin; FAI, free androgen index.

Parameters	Non –hyperandrogenic polycystic ovarian disease(n=33)	p-value
Metabolic variables		
Age (years)	23.9+/-5.5	0.861
Body Mass Index(Kg/m^2)	20.1+/-1.9	0.164
Waist circumference (cm)	66.6+/-5.5	0.566
Hirsutism clinical score	3(0-5)	<0.001
Systolic Blood Pressure measurement(mm/Hg)	113.0+/-9.5	0.767
Diastolic Blood Pressure measurement (mmHg)	75.4+/-6.3	0.963
Fasting blood glucose level (mg/dl)	85.6+/-5.2	0.385
HOMA -IR	1.79(1.47-2.16)	0.996
75 gram oral glucose tolerance test blood glucose level	97.7+/-2.09	0.221
75 gram oral glucose tolerance test insulin level	38.9(30.5-49.5)	0.38
Total cholesterol level (mg/dl)	174.9+/-30.0	0.868
Triglyceride level (mg/dl)	79.3+/-29.1	0.621
HDL serum cholesterol level(mg/dl)	66.7+/-17.7	0.683
LDL serum cholesterol level(mg/dl)	94.8+/-24.5	0.929
Hemoglobin A1C (%)	5.36+/-0.27	<0.001
Uric acid (mg/dl)	4.45+/-0.66	0.172
Hormonal parameters		
Total serum testosterone level (ng/ml)	0.32(0.28-0.36)	0.006
Free serum testosterone level	0.76(0.64-0.91)	0.006
SHBG(nmol/L)	55.3(47.2-64.8)	0.09
Free Androgen Index	1.98(1.66-2.37)	0.003
Lutenizing hormone (IU/L)	8.6(6.0-12.4)	0.978
Follicle Stimulating Hormone (iu/L)	5.4(4.4-6.6)	0.557
Estradiol(pg/ml)	26.9(19.2-37.7)	0.308
Visfatin(ng/ml)	2.69(2.06-3.52)	0.038

Hyper androgenic patients had significantly higher mean hemoglobin A1C levels, but mean levels of other metabolic variables were similar between the 2 groups. Although both groups had similar body mass index and waist circumference, significantly higher serum visfatin levels were observed in hyper androgenic patients than those in non-hyper androgenic patients (mean level of serum visfatin was 3.87 [95% CIs, 3.09-4.85] ng/mL in hyper androgenic patients and 2.69 [95% CIs, 2.06-3.52] ng/mL in non-hyper androgenic patients, respectively; P=0.038). Finally, the correlations between serum visfatin levels and various parameters were evaluated. In women with PCOS, serum visfatin levels positively correlated with BMI (r=0.23; P=0.047) and log FAI (r=0.27; P=0.021) and negatively correlated with HDL cho-

lesterol levels (r=−0.37; P=0.025) (Fig. 1). Except HDL cholesterol levels (r=−0.10; P=0.597), correlations between serum visfatin levels and BMI (r=0.40; P=0.021) or log FAI (r=0.27; P=0.023) were also observed in the controls. All other parameters, such as IR markers, SHBG, TG, and LDL cholesterol levels, showed no correlations with visfatin levels in both the patients and the controls (data not shown).

6. Discussion

The goal of current research study performed is to compare and contrast visfatin serum levels among polycystic ovarian disease in non-obese females and matched research control group and additionally to evaluate statistical correlation concerning serum levels of visfatin and different obtained parameters. As regards the data and indices obtained from the current research study, visfatin serum levels are observed to be nearly similar between both research group categories the polycystic ovarian disease and normal controls. On the other hand, females having polycystic ovarian disease had statistically significant greater visfatin indices in their serum that was a prominent finding that was reveled in cases classified in the group of hyperandrogenism than cases grouped in the non-hyperandrogenic category. Serum Visfatin displayed positive statistical correlation with Body Mass Index and log Free Androgen Index and a negative statistical correlation with serum HDL cholesterol measurements. According to the fact that poly cystic ovarian disease is featured by dysfunctional secretory pattern of adipokinestriggering inflammatory cascades and pathways and insulin resistance at molecular levels, the raise in serum visfatin measurements in hyperandrogenic class of polycystic ovarian disease cases or its statistical correlation with serum androgen levels could imply a correlation between hyperandrogenic feature in females suffering PCO with elevated serum visfatin [12-14]. Correlation between visfatin serum levels and females with PCO Is a matter of research studies debate with contradictory results requiring future large scale studies to be performed with meta analysis to verify usefulness and clinical significance. An amount of prior research studies performed have mentioned that females suffering PCO have greater serum visfatin levels than that observed in Body Mass Index –matched controls or unmatched research control subjects. Additionally serum visfatin indices in PCO cases with normal-weight have been revealed to be greater in levels than that observed in control subjects with obesity [15-17]. Conversely visfatin serum levels are similar between females with polycystic ovarian disease and body mass index -matched or unmatched research control subjects. One of the facts that need to be investigated is that hyperandrogenic and non-hyperandrogenic females with polycystic ovarian disease could vary in their metabolic features. In the current research study, greater visfatin levels are displayed in hyperandrogenic cases more than non-hyperandrogenic cases, additionally serum vis-fatin had a positive statistical correlation with log free androgen index (r=0.27; P=0.021) in Polycystic ovarian disease cases. A prior research group mentioned that serum visfatin levels are observed to be similar when comparing between females with and without poly cystic ovarian disease, but greater serum visfatin levels are observed in adolescents with hirsutism having polycystic ovarian disease in comparison to cases that have no hirsutism. In harmony with the research data of the current study prior research studies performed have mentioned that serum visfatin levels in correlation with testosterone serum levels (r=0.47; P=0.002) or free androgen index (r=0.48; P=0.002) in lean cases with poly cystic ovarian disease. Visfatin was considered to exert insulin-mimetic properties, and it is well known that hyperinsulinemia can stimulate ovarian androgen synthesis. Thus, observed correlation between visfatin and FAI in the current study may be associated with insulin-like action of visfatin. Nevertheless, the current study shows no direct correlation between visfatin and the index of IR such as fasting insulin, HOMA-IR or 75 g OGTT 2-hour insulin levels. Although the findings of this study do not show a correlation between visfatin and SHBG, Panidis et al. reported that plasma visfatin levels were negatively correlated with SHBG levels in normal-weight women with PCOS. There are no data regarding the direct role of visfatin in SHBG production in liver, but the correlation between visfatin and FAI may stem from the association between visfatin and SHBG. Although the current study was performed on non-obese subjects, the common influence of obesity, which might be related with both visfatin and free androgen index, cannot be completely ruled out. Further studies are required to clarify whether visfatin may be a marker of hyperandrogenemia in women with PCOS [18-20]. Visfatin negatively correlated with HDL cholesterol levels in women with PCOS. In contrast with the current study, a previous study reported that visfatin levels showed positive correlation with HDL cholesterol levels in lean PCOS patients. This may indicate that visfatin is associated with lipid homeostasis in lean women with PCOS, but the direction of association remains unclear [21].

7. Conclusion

In the current research study implies that there were no statistically significant differences in levels of visfatin measured in serum between cases of polycystic ovarian disease and the matched research control subjects. On the other hand, cases with hyperandrogenism displayed statistically significant greater visfatin serum levels than cases with non-hyperandrogenism, and additionally serum levels of visfatin had a positive statistically correlation with log Free Androgen Index. Additional future research

should consider racial and ethnic differences with larger sample size considering more variables of interest to reveal clinical relevance of visfatin and integration in clinical guidelines practice as a potential biological marker for PCO, Hyperandrogenism and various possible clinically related issues.

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