Original Study

# Plasma Visfatin Levels in Adolescents with Polycystic Ovary Syndrome: A Prospective Case-Control Study

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A B S T R A C T

*Study Objective:* We evaluated the plasma visfatin levels in hirsute female adolescents with polycystic ovary syndrome.
*Design, Setting, and Participants:* This prospective case-control study included 87 female patients who were seen in our adolescence department. Demographic characteristics and hormonal and biochemical parameters were evaluated between patients with and without polycystic ovary syndrome. Next, we divided the patients with polycystic ovary syndrome into the following subgroups: overweight or obese (body mass index [BMI] $\geq$ 25 kg/m$^2$) vs normal weight (BMI $<$ 25 kg/m$^2$) and hirsute vs nonhirsute.
*Results:* There were statistically significant differences in the BMI, serum androgen levels, homeostasis model assessment–insulin resistance (HOMA-IR) levels, and insulin levels between patients with and without polycystic ovary syndrome ($P < .05$). The mean visfatin levels showed no statistically significant difference between these 2 groups ($P > .05$). The serum visfatin levels were similar between the 2 subgroups classified by BMI ($P > .05$). However, there were statistically significant differences in the total and free testosterone levels, 17-hydroxylase progesterone level, HOMA-IR level, and visfatin level between the 2 subgroups classified by hirsutism ($P < .05$). The plasma visfatin level was higher in hirsute PCOS than in nonhirsute PCOS patients.
*Conclusion:* Significantly higher visfatin levels were found in hirsute than in nonhirsute adolescents with PCOS. According to these results, plasma visfatin levels may be a useful marker in hirsute adolescents with PCOS.
*Key Words:* Polycystic ovary syndrome, Visfatin, Body mass index, Hirsutism

## Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrinological disorder causing anovulation-related menstrual problems. PCOS has a prevalence of 6%-8% in the general population.[1] Despite multiple discussions, no consensus on the most optimal diagnostic criteria has been reached.[2,3] Most gynecologists use the Rotterdam criteria (2 of the 3 following criteria: oligo-ovulation or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries) determined by the European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine for PCOS diagnosis.[4] However, it is more difficult to diagnose PCOS in adolescent girls. Almost 40% of teenaged girls have polycystic ovaries on ultrasound examination[1]; therefore, all 3 criteria are considered to be necessary for a diagnosis of PCOS in adolescent girls. For adolescent patients, the use of serum markers is important to achieve a diagnosis of PCOS.[5] Because of this, for adolescent girls, the use of nonandrogen serum markers could be valuable to achieve a diagnosis of PCOS.

Previous studies have evaluated different serum markers for the diagnosis of PCOS, including anti-Müllerian hormone,[6] adiponectin,[7] leptin,[8] and visfatin.[9] Visfatin, also termed pre–B-cell colony-enhancing factor, is a 52-kDa cytokine expressed and secreted by lymphocytes. Visfatin levels are reportedly increased in patients with type 2 diabetes, obesity, PCOS, and nonalcoholic fatty liver disease.

In the present study, we compared plasma visfatin levels and their association with clinical parameters between adolescents with and without PCOS.

## Methods

This prospective case-control study was performed at Zekai Tahir Burak Women's Health Education and Research Hospital in Ankara, Turkey, between June 2013 and December 2013. The study was performed in accordance with the Helsinki Declaration and was approved by the Ethics Committee of Zekai Tahir Burak Women's Health Research and Education Hospital.

A total of 87 female patients aged 16-20 years (49 patients with PCOS and 38 controls without PCOS) visited our adolescence department during the study period. PCOS was diagnosed according to the Rotterdam consensus criteria (2 of the following 3 criteria: oligo-ovulation or anovulation, clinical and/or biochemical signs of hyperandrogenism, and polycystic ovaries).[4] The hirsutism score was evaluated by the same clinician according to the modified Ferriman–Gallwey scoring system.[10,11] Ultrasound evaluation of polycystic ovaries was performed by a single clinician (Aloka Co, Tokyo, Japan). The patients included in the study did not have thyroid abnormalities, diabetes

The authors indicate no conflicts of interest.

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mellitus, hyperprolactinemia, Cushing syndrome, coronary artery disease, or alcohol or drug use. The control group consisted of patients without PCOS who had been admitted for vaginal and urinary system infections.

Following a detailed history and physical examination, the clinical information evaluated included age, body mass index (BMI, in kg/m$^2$), Ferriman–Gallwey score (FGS), and the levels of follicle-stimulating hormone, luteinizing hormone (LH), estradiol, prolactin, total and free testosterone, dehydroepiandrosterone sulfate, androstenedione, 17-hydroxylase (17-OH) progesterone, thyroid-stimulating hormone, insulin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total cholesterol, total triglyceride, homeostasis model assessment–insulin resistance (HOMA-IR),[12] and visfatin.

Blood samples were obtained from adolescents during the early follicular phase (3-5 days) of their spontaneous menstrual cycle or progesterone-induced menstrual cycle in the presence of amenorrhea. The waist circumference was measured as the smallest circumference at the level of the umbilicus. The hip circumference was measured as the widest circumference at the level of the buttocks.

The insulin, testosterone, follicle-stimulating hormone, LH, estradiol, prolactin, and thyroid-stimulating hormone levels were measured using the Advia Centaur XP Immunoassay (Siemens, Erlangen, Germany). The 17-OH progesterone level was measured by using an enzyme-linked immunosorbent assay (ELISA) (17-OHP Elisa kit; MyBioSource Inc., San Diego, CA). The plasma visfatin level was measured by using a commercially available ELISA kit (Human EIA kit; RayBiotech, Inc., Norcross, GA) according to the manufacturer's protocol, with a coefficient of variation of less than 10%. The insulin sensitivity was determined by the HOMA index using the following formula: HOMA-IR = (insulin at baseline [pmol/L] × glucose at baseline [mmol/L]).[13]

The patients were first divided into the PCOS and non-PCOS groups. Then we divided the PCOS group into the following subgroups: overweight or obese (BMI ≥ 25 kg/m$^2$, n = 18; 5 overweight and 13 obese) vs normal weight (BMI < 25 kg/m$^2$, n = 31) and hirsute (n = 32) vs non-hirsute (n = 17).

*Statistical Analysis*

The mean and standard deviation were calculated for continuous variables. The normality of the variables was analyzed by using the Kolmogorov–Smirnov test. Student's *t* test and the Mann–Whitney *U* test were used to evaluate associations between the categorical and continuous variables. The receiver operating characteristics (ROC) curve analysis method was performed to identify the cut-off values and discriminative roles of statistically significant variables in the subgroups. All variables were included in the backward stepwise procedure. Two-sided *P* values were considered statistically significant at $P < .05$. Statistical analyses were carried out using SPSS 15.0 for Windows (SPSS Inc, Chicago, IL).

## Results

The clinical and demographic features of the patients in the PCOS group (n = 49) and non-PCOS control group (n = 38) are shown in Table 1. The mean patient age was similar between the 2 groups. The BMI was significantly higher in the PCOS group ($P < .05$). The mean androstenedione, total and free testosterone, 17-OH progesterone, and HOMA-IR levels were significantly higher in the PCOS group ($P < .05$). The mean visfatin levels showed no statistically significant difference between the groups.

Table 2 shows the results of the subgroup analysis of patients with PCOS classified by BMI: overweight or obese (BMI ≥ 25 kg/m$^2$, n = 18) vs normal weight (BMI < 25 kg/m$^2$, n = 31). The mean hormonal parameters and visfatin levels, with the exception of the serum LH levels, were higher in obese than in nonobese patients with PCOS; however, only the HOMA-IR level was significantly different between the 2 groups (Table 2). Table 3 shows the results of the comparison of the hirsute PCOS group and the non-PCOS control group. The mean total and free testosterone, LH, estradiol, 17-OH progesterone, HOMA-IR, and visfatin levels were significantly higher in the hirsute PCOS group than in the non-PCOS control group ($P < .05$). The second subgroup of patients with PCOS was classified into 2 groups according to their hirsutism score. Patients with an FGS of

**Table 1**
Clinical and Demographic Features of the Patients in the PCOS and Non-PCOS Control Groups

| Variables | PCOS Group (n = 49) | Non-PCOS Control Group (n = 38) | *P* |
|---|---|---|---|
| Age, y | 18.80 ± 2.20 | 19.61 ± 2.41 | .101 |
| BMI, kg/m$^2$ | 24.06 ± 5.22 | 21.30 ± 3.89 | .003 |
| WHR | 0.74 ± 0.05 | 0.73 ± 0.044 | .347 |
| DHEAS, μg/dL | 266.5 ± 103.83 | 244 ± 74.18 | .268 |
| Androstenedione, ng/mL | 2.70 ± 0.99 | 1.76 ± 0.65 | <.001 |
| Free testosterone, ng/dL | 2.82 ± 0.94 | 1.73 ± 0.42 | <.001 |
| Total testosterone, ng/dL | 51.04 ± 24.10 | 39.42 ± 15.38 | .008 |
| FSH, mIU/mL | 5.87 ± 1.62 | 6.10 ± 1.39 | .411 |
| LH, mIU/mL | 7.46 ± 4.72 | 5.19 ± 1.55 | .077 |
| $E_2$, pg/mL | 41.65 ± 18.17 | 40.86 ± 11.46 | .807 |
| Prolactin, ng/mL | 14.79 ± 7.05 | 12.88 ± 5.45 | .377 |
| 17-OHP, ng/mL | 1.31 ± 0.42 | 1.12 ± 0.42 | .017 |
| TSH, mIU/mL | 2.15 ± 0.95 | 1.86 ± 1.07 | .063 |
| HOMA-IR | 3.57 ± 2.49 | 2.37 ± 1.53 | .004 |
| Visfatin, ng/mL | 63.09 ± 15.23 | 61.31 ± 14.10 | .579 |

BMI, body mass index; DHEAS, dehydroepiandrostenedione sulfate; E2, estradiol; FSH, follicle-stimulating hormone; HOMA-IR, homeostatic model assessment–insulin resistance; LH, luteinizing hormone; OHP, hydroxy progesterone; T, testosterone; TSH, thyroid-stimulating hormone; WHR, waist:hip ratio.