J Endocrinol Invest (2017) 40:487–497
DOI 10.1007/s40618-016-0582-x

ORIGINAL ARTICLE

# Visceral adiposity index levels in overweight and/or obese, and non-obese patients with polycystic ovary syndrome and its relationship with metabolic and inflammatory parameters

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Received: 23 September 2016 / Accepted: 7 November 2016 / Published online: 12 November 2016


**Abstract**
*Background* Visceral adiposity index (VAI) is a proposed parameter to evaluate visceral obesity instead of waist circumference (WC) in patients with polycystic ovary syndrome (PCOS). We aimed to evaluate VAI levels in overweight and/or obese, and non-obese PCOS patients and investigate the association between metabolic and inflammatory parameters.
*Methods* Seventy-six PCOS patients between 18 and 40, and 38 age- and BMI-matched controls were enrolled into the study. Both PCOS groups and controls were classified into two subgroups according to body mass index (BMI) <25 and ≥25 kg/m$^2$.
*Results* In PCOS patients, waist/hip ratio (WHR) ($p = 0.023$), diastolic blood pressure (DBP) ($p = 0.001$), insulin ($p = 0.011$), homeostasis of model assessment (HOMA-IR) ($p = 0.006$) and uric acid (UA) ($p = 0.002$) were higher than controls. In overweight and/or obese PCOS group, DBP ($p < 0.001$), insulin ($p = 0.002$), HOMA-IR ($p = 0.001$), triglyceride ($p = 0.015$) and VAI ($p = 0.031$) were higher than overweight and/or obese controls. In non-obese PCOS group, WHR ($p = 0.016$), WC ($p = 0.030$), DBP ($p = 0.010$) and UA ($p < 0.001$) were higher than non-obese controls. Similar VAI levels were found in all PCOS and non-obese PCOS subgroups than peer controls. Overweight and/or obese PCOS group had higher VAI levels than non-obese PCOS group ($p < 0.001$). VAI levels were positively correlated with WHR, glucose, HOMA-IR, high-sensitive CRP and UA in PCOS group. In controls, VAI levels were positively correlated with WHR, insulin and HOMA-IR.
*Conclusion* We found that VAI levels were higher in overweight and/or obese PCOS patients compared to peer controls and non-obese PCOS patients, and associated with some metabolic and inflammatory parameters.

**Keywords** Polycystic ovary syndrome · Waist circumference · Visceral adiposity index · Insulin resistance · High-sensitive CRP · Uric acid

## Introduction

Polycystic ovary syndrome (PCOS) is a common endocrinological disorder among women at reproductive age with a worldwide prevalence of 5–20% [1]. The characteristics of this syndrome are known as clinical and biochemical hyperandrogenism, ovulatory dysfunction and polycystic ovarian appearance [1]. In addition to these characteristics, increased central and visceral adiposity, obesity, insulin resistance (IR) and impaired glucose tolerance (IGT), diabetes mellitus (DM), dyslipidemia, hypertension (HT), metabolic syndrome (MetS), endothelial dysfunction and increased inflammation/pro-inflammatory status are other well-known features of the syndrome [1–5].

In PCOS patients, visceral adiposity plays an important role in the development of PCOS and its associated metabolic disturbances, and is encountered in both normal and overweight patients with PCOS [6, 7]. It is a well-known fact that central obesity is associated with a number of

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metabolic disturbances, including IR, type 2 DM, dyslipidemia and hypertension, and is a predictor for the development of cardiovascular morbidity and mortality [8–10]. It is also known that the assessment of central/visceral adiposity is a better evaluation, compared to the assessment of overall obesity in predicting cardiovascular disorders (CVDs) [11]. In clinical practice, body mass index (BMI) is a commonly used measurement in order to evaluate obesity, but shows no linear association with body fat percentage. In addition, such features as gender, race, hydration status and body muscle mass are known to have effects on BMI [12]. As a predictor of metabolic and CVDs, central obesity can be measured easily through waist circumference (WC). In the definition of MetS, WC has replaced with BMI [13], but it should be kept in mind that volumes of both subcutaneous and visceral adipose tissues determine the measurement of WC. Metabolic disturbances have a stronger association with visceral adipose tissue than subcutaneous adipose tissue [14]. However, fat content of subcutaneous adipose tissue on waist may vary from person to person and can also be affected, depending on the differences of ethnicity and gender. Because visceral adipose tissue, but not subcutaneous, plays a significant role in the development of IR, CVD or other metabolic disturbances, the differentiation of true visceral adiposity from central or abdominal type of obesity is important. For this reason, in the investigation of visceral adiposity, the International Diabetes Federation recommends that computerized tomography (CT) or magnetic resonance imaging (MRI) be used as significant screening tools [15]. Recommended to evaluate visceral fat tissue, all these methods, such as CT, MRI and dual-energy X-ray absorptiometry (DXA), have yet to be used in routine clinical practice because of higher fiscal burdens and radiation risks [16, 17]. As an indicator of the functions of visceral adipose tissue, the visceral adiposity index (VAI) has been adopted and successfully used in predicting IR and cardiometabolic risk factors in patients with PCOS and general population [18–25]. VAI levels are calculated easily by a mathematical formula using anthropometric [body mass index (BMI) and WC] and biochemical [high-density lipoprotein (HDL) cholesterol and triglyceride (TG)] parameters [19]. VAI has been proposed as a useful tool to detect early and to evaluate cardiometabolic risks before MetS develops to overt type in metabolically unhealthy patients with PCOS [20].

Contrary to studies reporting positive results, there are also studies reporting that as a measurement parameter, VAI is deficient in predicting IR, compared to other measurable parameters such as BMI and WC in patients with PCOS and general population [10, 26].

While we were designing this study, no other studies evaluating VAI levels in overweight and/or obese and non-obese PCOS patients were encountered in the literature, to the best of our knowledge. However, a similarly designed study aiming to assess VAI levels in obese and non-obese PCOS patients was published a few months ago by Un et al. [27]. In their study, VAI, TG, high-density lipoprotein-cholesterol (HDL-cholesterol), homeostasis of model assessment-insulin resistance (HOMA-IR) and high-sensitive C-reactive protein (hsCRP) levels were found to be similar in all PCOS patients, compared to controls. After their re-classification of the cases into two subgroups as obese and non-obese, obese PCOS patients were observed to have higher VAI, TG, HOMA-IR and hsCRP, and lower HDL-cholesterol levels, compared to non-obese PCOS patients. However, the researchers published no results of their obese and non-obese subgroups, compared to their peer healthy controls.

In the present study, we aimed to investigate VAI levels and its correlations with clinical, metabolic and inflammatory parameters in overweight and/or obese, and non-obese PCOS patients, and age- and BMI-matched controls.

## Materials and methods

This prospective study was conducted in the division of endocrinology in Konya Health Application and Research Center, University of Health Sciences (previously entitled as Konya Training and Research Hospital) between June 2015 and August 2016. Informed consents were obtained from all participants. The study protocol was approved by the ethics committee of Meram Medical Faculty of Necmettin Erbakan University.

Overweight and/or obese PCOS patients with BMI $\geq$25 kg/m$^2$ ($n$ = 38) and non-obese PCOS patients with BMI <25 kg/m$^2$ ($n$ = 38) were enrolled into the study. Age- and BMI-matched 20 overweight and/or obese and 18 non-obese healthy subjects were included into the study as the control group. All patients were aged between 18 and 40 years.

The diagnosis of PCOS was formed on the Rotterdam criteria with at least two of the following three criteria: the existence of oligomenorrhea (cycles lasting longer than 35 days) or amenorrhea (less than 2 menstrual cycles in the past 6 months), clinical or biochemical hyperandrogenism and polycystic appearance of ovary on ultrasonography (USG), when other causes of hyperandrogenism, such as Cushing's syndrome, congenital adrenal hyperplasia or virilization, were excluded [28]. Subjects taking drugs interfering with or affecting IR, UA and inflammation, such as estrogens, oral contraceptives, corticosteroids, immunosuppressants, antihyperlipidemics, antihypertensive drugs, thiazide, antihyperglycemic drugs, UA lowering drugs and insulin sensitizing drugs in the last 6 months, and anti-inflammatory drugs in the last month, or those with any

known active infection, inflammatory diseases, such as Crohn's, ulcerative colitis, rheumatoid arthritis, systemic lupus erythematosus or benign or malignant hematologic disorders, any solid tissue cancers, hypertension or exposed to any surgical intervention within the past 6 months, were excluded from the study.

Height (m) and weight (kg) were measured with underwear clothing. WC was measured as the minimum size between iliac crest and lateral costal margin. Hip circumference (HC) was measured at the widest point over the buttocks. Waist/hip ratio (WHR) was calculated as WC divided by HC. BMI was calculated as weight (kg)/height square ($m^2$).

All blood samples were drawn after an overnight fasting between third and fifth days of menstruation, being separated by centrifugation and stored in deep freeze at −70 °C until being analyzed.

Glucose levels [normal range (NR), 70–105 mg/dL] were measured using the hexokinase method with Olympus AU 5800 device (Beckman Coulter Inc., CA, USA). Insulin levels [(NR), 6–27 μlU/mL] were measured using the chemiluminescence method with an Immulite 2000 device (Siemens Healthcare Diagnostics, NJ, USA). The analytic sensitivity of the assay was 2 μlU/mL. Intra-assay variations as CV for various insulin values were 5.5% (7.67 μlU/mL), 4.0% (12.5 μlU/mL), 3.3% (17.2 μlU/mL), 3.9% (26.4 μlU/mL), 3.8% (100 μlU/mL) and 3.7% (291 μlU/mL). Inter-assay variations for the insulin concentrations mentioned in the previous statement were 7.3, 4.9, 4.1, 5, 4.2 and 5.3%, respectively. The levels of HDL-cholesterol [(NR), 40–90 mg/dL] were measured with immune reaction (antigen–antibody complex) using an Olympus AU 5800 device (Beckman Coulter Inc., CA, USA), and TG levels [(NR), 0–200 mg/dL] were measured using a routine enzymatic method with an auto analyzer, Olympus AU 5800 device (Beckman Coulter Inc., CA, USA). UA levels [(NR), 2.6–6 mg/dL] were measured by Olympus AU 5800 (Beckman Coulter Inc., CA, USA) with enzymatic uricase method, while hsCRP levels [(NR), 0–3 mg/L] were measured with Siemens Health Care Diagnostic BN II (Siemens Health Care Diagnostic, Marburg, Germany) with the nephelometric method. IR was calculated by HOMA-IR based on the following formula [fasting plasma glucose (mmol/L) × fasting serum insulin (μIU/mL)/22.5]. VAI levels were calculated for women by the formula, (WC/[36.58 + (1.89 × BMI)]) × [(TG (mmol/L)/0.81) × (1.52 × HDL-cholesterol (mmol/L))] [19].

### Statistical analyses

The statistical analyses of the data were carried out with SPSS v21 statistical software package. The normality of the data was analyzed with the Shapiro–Wilk test. The descriptive statistics for variables with normal distribution of continuous data [mean ± standard deviation (SD)] and with no normally distributed variables [median (minimum:maximum)] were indicated. The independent-samples *t* test was used in the comparison of two independent samples for normally distributed continuous data, and for not normally distributed continuous data, the Mann–Whitney *U* test was used in the comparison of two independent groups. The Spearman's correlation coefficient was performed to determine the relationship between not normally distributed variables, while the Pearson's test was used to detect the relationship between normally distributed variables. $p \leq 0.05$ was accepted as significant. Statistically significant values are indicated in bold in tables.

## Results

The anthropometric, biochemical and metabolic characteristics of patients are summarized in Table 1. Before subgroup analyses of overweight and/or obese and non-obese PCOS patients, our participants were compared in two main groups as patients with all patients with PCOS ($n = 76$) and controls ($n = 38$). Compared with controls, all patients with PCOS had significantly higher WHR, diastolic blood pressure (DBP), modified Ferriman–Gallwey (mFG) score, insulin, HOMA-IR and UA levels. The levels of glucose, lipid profile, hsCRP and VAI shown in Fig. 1 were similar in both groups.

Presented in Table 2, the levels of VAI were found to be positively correlated with WHR, insulin, glucose, HOMA-IR, UA and hsCRP levels in all patients with PCOS, while demonstrated to be positively correlated with WHR, insulin and HOMA-IR levels in controls.

### Subgroup analyses

The anthropometric, biochemical and metabolic characteristics of the subgroups are summarized in Table 3.

In the comparison of overweight and/or obese PCOS patients ($n = 38$) and controls ($n = 20$), overweight and/or obese PCOS group had higher DBP, mFG score, insulin, HOMA-IR, TG and VAI levels (Fig. 1). Glucose, HDL-cholesterol, UA and hsCRP levels were similar in overweight and/or obese PCOS, and overweight and/or obese control groups. Given the formula of VAI calculated with WC, BMI, HDL-cholesterol and TG, and the similar levels of WC, BMI and HDL-cholesterol in overweight and/or obese PCOS, and overweight and/or obese control groups, higher VAI levels in overweight and/or obese PCOS group were considered to arise from higher TG levels. In the comparison of non-obese PCOS patients ($n = 38$) and

non-obese controls ($n = 18$), non-obese PCOS group was found to have higher WC, WHR, DBP, mFG and UA levels. Glucose, insulin, lipid parameters, HOMA-IR, VAI (Fig. 1) and hsCRP levels were detected to be similar in non-obese PCOS patients and non-obese controls.

In the comparison of overweight and/or obese, and non-obese PCOS groups, overweight and/or obese PCOS group was detected to have higher BMI, WC, HC, WHR, systolic blood pressure (SBP) and DBP, glucose, insulin, HOMA-IR, TG, UA, hsCRP and VAI levels (Fig. 1), compared to non-obese PCOS; however, HDL-cholesterol levels were detected higher in non-obese PCOS group, compared to overweight and/or obese PCOS. mFG scores were found similar in overweight and/or obese and non-obese PCOS groups.

In the correlation analyses of overweight and/or obese PCOS group, VAI levels were positively correlated with WHR, insulin, HOMA-IR and UA levels (Table 4). In non-obese PCOS group, VAI levels were positively correlated with WHR, insulin and HOMA-IR levels.

Based on the presence of obesity, our cases were re-divided into two main groups as non-obese (BMI < 25 kg/m$^2$) and overweight or obese (BMI ≥ 25 kg/m$^2$) cases by including both PCOS patients and controls in each group. Higher hsCRP levels were found in overweight and/or obese group, compared to non-obese group (3.169 ± 3.410 vs. 1.042 ± 2.13 mg/L, respectively, $p < 0.001$).

## Discussion

In the present study, VAI levels were found similar in all patients with PCOS and controls. After the cases were divided into subgroups, overweight and/or obese patients with PCOS were found to have higher VAI levels, compared to BMI-matched controls and non-obese PCOS.

Given the formula of VAI, WC, BMI, TG and HDL-cholesterol levels are known to be influential on VAI levels [19]. In the present study, BMI values were determined to be similar in all patients with PCOS and controls, and PCOS subgroups, compared to peer controls. WC levels were similar in all patients with PCOS and controls, and overweight and/or obese PCOS groups, compared to overweight and/or obese controls. However, higher WC levels were detected in non-obese PCOS group, compared to non-obese controls. Although HDL-cholesterol levels were similar in both subgroups when compared to peer controls, overweight and/or obese PCOS group was found to have lower HDL-cholesterol levels than non-obese PCOS group. Also, overweight and/or obese PCOS group was observed to have higher TG levels, compared to overweight and/or obese controls and non-obese PCOS patients. Previous studies related to PCOS show that high TG, very low chain lipoprotein (VLDL), low-density lipoprotein (LDL) and low HDL-cholesterol levels are commonly seen in patients with PCOS [29–31], and these lipid profiles are also seen

**Table 1** Anthropometric, biochemical and metabolic characteristics of study population

| | PCOS ($n = 76$) | Controls ($n = 38$) | $p$ value |
|---|---|---|---|
| Age (year) | 23.00 (18:34) | 25.00 (18:38) | 0.619 |
| BMI (kg/m$^2$) | 25.38 (18.3:42.8) | 26.39 (18.7:38.4) | 0.544 |
| Weight (kg) | 72.36 ± 17.73 | 69.07 ± 14.23 | 0.556 |
| Waist circumference (cm) | 83.5 (56:115) | 82.5 (65:103) | 0.433 |
| Hip circumference (cm) | 105 (84:138) | 109 (90:137) | 0.201 |
| WHR | 0.79 ± 0.08 | 0.76 ± 0.05 | **0.023** |
| Systolic blood pressure (mmHg) | 106.51 ± 9.73 | 108.16 ± 8.65 | 0.277 |
| Diastolic blood pressure (mmHg) | 68.03 ± 6.64 | 61.84 ± 5.12 | **<0.001** |
| mFG score | 17.13 ± 5.95 | 3.45 ± 0.98 | **<0.001** |
| Glucose (mg/dL) | 87.5 (69:102) | 85.5 (58:102) | 0.151 |
| Insulin (μU/mL) | 9.4 (2:38) | 7.4 (2:22.4) | **0.011** |
| HOMA-IR | 2.1 (0.34:9.38) | 1.37 (0.4:5.64) | **0.006** |
| hsCRP (mg/dL) | 0.9 (0.16:14.9) | 0.74 (0.16:10) | 0.081 |
| Uric acid (mg/dL) | 4.7 (2.8:9.4) | 4.3 (2.6:7.5) | **0.002** |
| HDL-cholesterol (mg/dL) | 47.8 ± 9.84 | 50.45 ± 9.86 | 0.181 |
| Triglyceride (mg/dL) | 90.5 (33:258) | 72 (31:183) | 0.077 |
| VAI | 1.39 (0.48:5.93) | 1.16 (0.47:3.49) | 0.062 |

Results are given as: *mean* ± *standard deviation* and *median (minimum:maximum)*

Significant results are given in bold

*PCOS* polycystic ovary syndrome, *BMI* body mass index, *WHR* waist/hip ratio, *mFG* Ferriman–Gallwey score, *HOMA-IR* homeostasis of model assessment-insulin resistance, *hsCRP* high-sensitive C-reactive protein, *VAI* visceral adiposity index

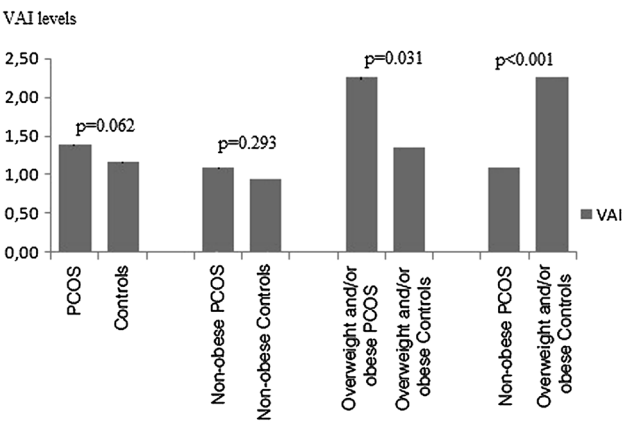


**Fig. 1** VAI levels in patients with PCOS and controls. *VAI* visceral adiposity index, *PCOS* polycystic ovary syndrome

**Table 2** Correlation analyses of some laboratory parameters in all PCOS patients and controls

| PCOS (*n*:76) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Controls (*n*:38) | WHR | Glucose | Insulin | HOMA-IR | UA | hsCRP | VAI |
| WHR | | | | | | | |
| *r* | 1.00 | −0.035 | 0.242 | 0.228 | 0.288 | 0.260 | 0.434 |
| *p* | | 0.761 | **0.035** | **0.048** | **0.012** | **0.023** | **<0.001** |
| Glucose | | | | | | | |
| *r* | 0.076 | 1.00 | 0.382 | 0.462 | −0.112 | 0.098 | 0.237 |
| *p* | 0.648 | | **0.001** | **<0.001** | 0.334 | 0.400 | **0.039** |
| Insulin | | | | | | | |
| *r* | 0.361 | 0.134 | 1.00 | 0.993 | 0.255 | 0.389 | 0.628 |
| *p* | **0.026** | 0.423 | | **<0.001** | **0.026** | **0.001** | **<0.001** |
| HOMA-IR | | | | | | | |
| *r* | 0.353 | 0.276 | 0.981 | 1.00 | 0.237 | 0.385 | 0.622 |
| *p* | **0.030** | 0.094 | **<0.001** | | **0.040** | **0.001** | **<0.001** |
| UA | | | | | | | |
| *r* | 0.373 | 0.038 | 0.050 | 0.081 | 1.00 | 0.347 | 0.361 |
| *p* | **0.022** | 0.819 | 0.765 | 0.630 | | **0.002** | **<0.001** |
| hsCRP | | | | | | | |
| *r* | 0.634 | 0.054 | 0.113 | 0.114 | 0.440 | 1.00 | 0.280 |
| *p* | **<0.001** | 0.748 | 0.498 | 0.496 | **0.006** | | **0.014** |
| VAI | | | | | | | |
| *r* | 0.434 | −0.130 | 0.343 | 0.349 | 0.276 | 0.211 | 1.00 |
| *p* | **0.006** | 0.438 | **0.035** | **0.032** | 0.094 | 0.203 | |

Significant results are given in bold

*PCOS* polycystic ovary syndrome, *WHR* waist/hip ratio, *HOMA-IR* homeostasis of model assessment-insulin resistance, *UA* uric acid, *hsCRP* high-sensitive C-reactive protein, *VAI* visceral adiposity index

commonly in IR status. Both HDL-cholesterol and TG levels, but not LDL-cholesterol, are mainly associated with obesity in patients with PCOS [32, 33]. Considering these four parameters affecting VAI levels, TG levels were seen to be different between overweight and/or obese PCOS and overweight and/or obese control groups, and WC levels were also different between non-obese PCOS and non-obese control groups, although no statistically significant difference was found among the other parameters (Table 3). Considering VAI formula and the presence of similar WC, BMI and HDL-cholesterol levels in our overweight and/or obese PCOS and overweight and/or obese control groups, higher VAI levels in overweight and/or obese PCOS group are considered to arise from higher TG levels. Even if WC and BMI scores are observed to be similarly present in overweight and/or obese PCOS and overweight and/or obese control groups, we consider that higher TG values lead to an increase in the remarks of CVD risks in overweight and/or obese PCOS patients. Even though higher WHR levels are encountered in patients with PCOS, similar adipose tissue volume and distribution are observed on MRI [34]. So, such parameters as WHR levels indicating abdominal obesity may not reflect the volume and functions of adipocytes fully and accurately. In a study by Maddolini et al. [35] it was reported that VAI was significantly correlated with WHR, neck and wrist circumferences in patients with BMI $\geq$25 kg/m$^2$, although no association was found between VAI and body circumferences in patients with <BMI 25 kg/m$^2$. In another study designed similarly to our study by Un et al. [27], it was reported that VAI, HDL-cholesterol and TG levels were similar in all PCOS groups compared to all controls, but after dividing participants into subgroups according to their BMI values, overweight and/or obese PCOS group was observed to have higher VAI and TG levels, and lower HDL-cholesterol levels, compared to non-obese PCOS group. As a limitation of the study by Un et al., while only all PCOS groups were reported to be compared to all controls, and overweight and/or obese PCOS groups to be compared to non-obese PCOS group, they reported no information about the relationship between overweight and/or obese PCOS patients and overweight and/or obese controls, and between non-obese PCOS and non-obese control groups. As different from their study, we compared overweight and/or obese PCOS and non-obese PCOS patients with their peer controls and found that VAI levels were higher only in overweight and/or obese

**Table 3** Anthropometric, biochemical and metabolic characteristics of study population according to subgroups

| | Overweight and/or obese PCOS ($n = 38$) | Overweight and/or obese controls ($n = 20$) | $p$ value | Non-obese PCOS ($n = 38$) | Non-obese controls ($n = 18$) | $p$ value | $p$ value* |
|---|---|---|---|---|---|---|---|
| Age (year) | 24 (18:34) | 22.5 (18:38) | 0.676 | 21.5 (18:30) | 26 (18:31) | 0.123 | 0.061 |
| BMI (kg/m$^2$) | 31.2 (26.1:42.8) | 31.4 (25.9:38.4) | 0.423 | 22.5 (18.3:24.7) | 21.2 (18.8:24.2) | 0.114 | **<0.001** |
| Weight (kg) | 85.07 ± 1.61 | 80.2 ± 9.79 | 0.719 | 59.65 ± 6.72 | 56.72 ± 5.18 | 0.082 | **<0.001** |
| Waist circumference (cm) | 92 (46:115) | 93.580:103 | 0.566 | 74 (64:96) | 71 (65:81) | **0.030** | **<0.001** |
| Hip circumference (cm) | 112 (103:138) | 118 (107:137) | 0.201 | 99 (84:115) | 96 (90:110) | 0.325 | **<0.001** |
| WHR | 0.81 ± 0.09 | 0.78 ± 0.04 | 0.175 | 0.77 ± 0.06 | 0.73 ± 0.04 | **0.016** | **0.004** |
| mFG | 17.82 ± 6.40 | 3.2 ± 1.05 | **<0.001** | 16.45 ± 5.45 | 3.72 ± 0.826 | **<0.001** | 0.267 |
| SBP (mmHg) | 108.95 ± 10.8 | 111 ± 7.88 | 0.321 | 104.08 ± 7.87 | 105 ± 8.57 | 0.795 | **0.048** |
| DBP (mmHg) | 69.47 ± 5.54 | 61.5 ± 5.87 | **<0.001** | 66.58 ± 7.36 | 62.22 ± 4.27 | **0.010** | **0.037** |
| Glucose (mg/dL) | 89.5 (79:100) | 86 (58:102) | 0.064 | 85 (69:102) | 85.5 (72:102) | 0.765 | **0.016** |
| Insulin (μU/mL) | 14.3 (3.6:38) | 10.1 (2.6:22.4) | **0.002** | 7.5 (2:28.2) | 5.9 (2:15.6) | 0.210 | **<0.001** |
| HOMA-IR | 2.97 (0.72:9.38) | 2.19 (0.4:5.64) | **0.001** | 1.53 (0.34:5.29) | 1.26 (0.42:3.27) | 0.158 | **<0.001** |
| hsCRP (mg/L) | 2.24 (0.33:14.3) | 1.43 (0.16:10) | 0.137 | 0.57 (0.16:14.9) | 0.36 (0.16:2.6) | 0.118 | **<0.001** |
| Uric acid (mg/dL) | 5 (3.4:9.4) | 4.65 (2.9:75) | 0.126 | 4.6 (2.8:6.6) | 3.8 (2.6:4.8) | **<0.001** | **0.028** |
| HDL-cholesterol (mg/dL) | 44.82 ± 9.02 | 46.6 ± 8.63 | 0.234 | 50.79 ± 9.82 | 54.72 ± 9.58 | 0.164 | **0.016** |
| Triglyceride (mg/dL) | 113 (46:258) | 92 (40:182) | **0.015** | 69.5 (33:212) | 65 (31:183) | 0.792 | **<0.001** |
| VAI | 2.26 (0.66:5.93) | 1.36 (0.59:3.49) | **0.031** | 1.09 (0.48:5.26) | 0.95 (0.47:3.38) | 0.293 | **<0.001** |

Results are given as: *mean* ± *standard deviation* and *median (minimum:maximum)*

Significant results are given in bold

*PCOS* polycystic ovary syndrome, *BMI* body mass index, *WHR* waist/hip ratio, *mFG* modified Ferriman–Gallwey score, *HOMA-IR* homeostasis of model assessment-insulin resistance, *hsCRP* high-sensitive C-reactive protein, *VAI* visceral adiposity index

* Overweight and/or obese PCOS *vs* non-obese PCOS

**Table 4** Correlation analysis of some laboratory parameters in overweight and/or obese, and non-obese patients with PCOS

| Overweight and/or obese PCOS (*n*:38) | | | | | | | |
|---|---|---|---|---|---|---|---|
| Non-obese PCOS (*n*:38) | WHR | Glucose | Insulin | HOMA-IR | UA | hsCRP | VAI |
| WHR | | | | | | | |
| *r* | 1.00 | −0.101 | 0.151 | 0.121 | 0.095 | 0.054 | 0.420 |
| *p* | | 0.546 | 0.365 | 0.468 | 0.572 | 0.747 | **0.009** |
| Glucose | | | | | | | |
| *r* | −0.144 | 1.00 | 0.370 | 0.471 | −0.112 | 0.035 | 0.115 |
| *p* | 0.388 | | **0.022** | **0.003** | 0.504 | 0.833 | 0.491 |
| Insulin | | | | | | | |
| *r* | 0.043 | 0.345 | 1.00 | 0.987 | 0.283 | 0.210 | 0.446 |
| *p* | 0.799 | **0.034** | | **<0.001** | 0.085 | 0.207 | **0.005** |
| HOMA-IR | | | | | | | |
| *r* | 0.023 | 0.438 | 0.985 | 1.00 | 0.260 | 0.192 | 0.437 |
| *p* | 0.893 | **0.006** | **<0.001** | | 0.115 | 0.249 | **0.006** |
| UA | | | | | | | |
| *r* | 0.344 | −0.279 | −0.073 | −0.089 | 1.00 | 0.421 | 0.474 |
| *p* | **0.034** | 0.089 | 0.662 | 0.596 | | **0.009** | **0.003** |
| hsCRP | | | | | | | |
| *r* | −0.033 | −0.078 | 0.039 | 0.044 | 0.159 | 1.00 | 0.143 |
| *p* | 0.846 | 0.643 | 0.818 | 0.793 | 0.341 | | 0.392 |
| VAI | | | | | | | |
| *r* | 0.398 | 0.206 | 0.357 | 0.363 | 0.131 | −0.056 | 1.00 |
| *p* | **0.013** | 0.215 | **0.028** | **0.025** | 0.432 | 0.740 | |

Significant results are given in bold

*PCOS* polycystic ovary syndrome, *WHR* waist/hip ratio, *HOMA-IR* homeostasis of model assessment-insulin resistance, *UA* uric acid, *hsCRP* high-sensitive C-reactive protein, *VAI* visceral adiposity index

PCOS patients, compared to overweight and/or obese controls. In addition, as consistent with their findings, we also found higher VAI levels in overweight and/or obese PCOS patients, compared to non-obese PCOS patients. In the present study, when compared overweight and/or obese PCOS patients with non-obese PCOS patients, higher BMI, WC and TG levels, and lower HDL-cholesterol levels were found in overweight and/or obese PCOS patients. According to the formula of VAI, because the four parameters influencing VAI levels are different in overweight and/or obese and non-obese PCOS groups, it is likely that different VAI levels are detected.

In a study, Oh et al. [36] reported that VAI levels were positively correlated with visceral fat area measured by CT, and SBP, DBP, visceral to subcutaneous fat ratio and testosterone levels, while negatively correlated with insulin sensitivity evaluated by euglycemic hyperinsulinemic clamp, and asserted that VAI could be replaced with CT scanning in order to evaluate visceral adiposity. As different from their study, we evaluated no visceral fat tissue using any of the recommended methods [15–17], and so evaluating no relationships between VAI and true visceral fat tissue. This is one of the limitations in our study.

It is known that some phenotypes of PCOS have unfavorable effects on metabolic parameters [37, 38]. In a study evaluating the relationship between VAI levels and the severity of menstrual disorder, Androulakis et al. [39] reported that as VAI levels increase, the severity of anovulation, IR and inflammation also increase. In another study carried out by Amato et al. [40], it was shown that oligomenorrheaic phenotypes of PCOS had higher VAI levels, compared to other phenotypes. In a study, Bil et al. [37] divided patients with PCOS into 4 phenotypic groups and reported that the highest VAI levels were detected in patients with hyperandrogenemia and oligo/anovulation group, and VAI was the only predictor demonstrating the development of MetS in patients with PCOS. In another study, Amato et al. [20] evaluated BMI, WHR, VAI levels and the risk category developed by the Androgen Excess Society to distinguish metabolically healthy PCOS patients from unhealthy ones, found that there was only a significant association between metabolically unhealthy PCOS patients with VAI criteria and higher IR, and proposed that VAI was a useful tool for the early detection and evaluation of cardiometabolic risks before developing into an overt MetS in metabolically unhealthy patients with PCOS [20]. As another limitation

of our study, none of our study population were classified according to PCOS phenotypes.

Although VAI levels are well correlated with visceral fat content, there is no definitive value to be used to diagnose visceral adiposity. Optimal VAI cutoff point was reported as 1.79 in Korean women with PCOS [36] and between 1.92 and 2.52 in general male and female Caucasian Sicilian population [41]. In our study, we calculated no cutoff value, since the study was designed to compare VAI levels in overweight and/or obese and non-obese PCOS patients.

In the present study, similar HOMA-IR levels were found in non-obese PCOS group, compared to peer controls, although HOMA-IR levels were detected to be significantly higher in all PCOS patients and overweight and/or obese PCOS groups, compared to peer controls. We also found that compared to non-obese PCOS patients, HOMA-IR levels were higher in overweight and/or obese PCOS patients. PCOS patients are known to have various degrees of IR and insulin secretion deficiency, and these disturbances play an important role in the pathophysiology of PCOS. The obese patients with PCOS have more IR than obese non-PCOS patients; however, this finding related to non-obese PCOS patients remains controversial [42–46]. In their study, Un et al. [27] reported similar HOMA-IR levels in patients with PCOS, compared to controls, but when their participants were further divided as overweight and/or obese, and non-obese, only overweight and/or obese PCOS group was seen to have higher HOMA-IR levels than non-obese PCOS patients. In another study, Holte et al. [45] reported that similar insulin sensitivity rates were present in both patients with PCOS and controls with BMI 21 kg/m$^2$, while a decline was observed in PCOS group as BMI levels increased (e.g., insulin sensitivity rates decreased 35 and 70%, when BMI levels were 28 and 35 kg/m$^2$, respectively). Layegh et al. [47] reported higher HOMA-IR levels in obese PCOS patients, compared to non-obese group, but the percentage of IR patients (HOMA-IR > 2.3) remained similar in both groups. The fact that Layegh et al. included no controls into their study can be seen as a limitation. Amato et al. [48] reported that as an anthropometric parameter, VAI is superior to BMI and WC values to predict the presence of impaired fasting glucose, IGT or DM in patients with PCOS. In other studies, VAI levels were reported to be positively correlated with HOMA-IR [39] and negatively correlated with glucose utilization during euglycemic hyperinsulinemic clamp test [36]. As consistent with other studies, VAI levels were positively correlated with HOMA-IR in all PCOS patients and subgroups in our study.

The predictive value of VAI, BMI, WHR and waist-to-height ratio (WHtR) was investigated to predict MetS in PCOS patients in a study performed by Techatraisak et al. [24] in Thailand, and VAI was reported to be the best parameter in predicting the presence of MetS, followed by BMI and WHtR. Moreover, cutoff points for optimal BMI value and VAI levels were reported as ≥28 kg/m$^2$ and 5.6 to detect the development of MetS in Thai women, respectively. On the other hand, Janghorbani et al. [25] reported VAI as a measurement method catching similar success levels to BMI, WC, WHR and WHtR in order to predict of DM. As different from other studies, Glintborg et al. [10] reported that although patients with PCOS had elevated LAP and VAI levels, the best predictor of HOMA-IR in patients with PCOS was trunk fat, WC and BMI levels, and VAI fell behind the other parameters in predicting HOMA-IR. Likewise, in a recent article performed by Borruel et al. [26], WC and BMI measurements were reported to be a more accurate and reliable marker to detect of visceral adiposity and a good indicator of IR and hepatic steatosis, compared to VAI levels.

In the present study, similar hsCRP levels were found in all PCOS and subgroups, compared to peer controls. In addition, overweight and/or obese PCOS group had higher hsCRP levels, compared to non-obese PCOS. However, when the cases were re-classified into two primary groups as BMI <25 kg/m$^2$ and BMI ≥25 kg/m$^2$, the cases with BMI ≥25 kg/m$^2$ (including PCOS and controls) were seen to have higher hsCRP levels, compared to non-obese patients with BMI <25 kg/m$^2$. In addition, similar difference was also found in subgroups (overweight and/or obese PCOS vs non-obese PCOS, and overweight and/or obese controls vs non-obese controls). In the literature, it is well established that increased subclinical inflammation is one of the characteristics of PCOS [49, 50]. On the other hand, Un et al. [27] reported similar hsCRP levels in PCOS patients, compared to controls. After the patients were re-classified according to the presence of the overweight and/or obesity (BMI ≥ 25 kg/m$^2$), it was reported that overweight and/or obese patients with PCOS had higher hsCRP levels, compared to non-obese patients with PCOS, and it was concluded that obesity was the major factor affecting hsCRP levels in patients with PCOS. In other studies, similar results were reported [51, 52]. In another study, Puder et al. [50] reported that increased hsCRP and IR levels were mainly associated with increased visceral obesity rather than the presence of PCOS. In a study performed in Korean patients with PCOS, Jeong et al. [53] reported that HbA1c, hs-CRP, lipid accumulation product and TG could be used for detecting abnormal glucose tolerance and that cutoff level for hsCRP levels was 1.16 mg/dL (70.3% sensitivity and 80.1% specificity).

VAI levels are associated with subclinical low-grade inflammation in patients with PCOS. Amato et al. [54] reported that VAI levels were correlated with hsCRP and other adipocytokine levels. In our study, only PCOS groups (including overweight and/or obese, and non-obese)

showed a positive correlation between VAI and hsCRP levels. In subgroup analysis, no correlation was found between VAI and hsCRP levels. We consider that further studies are needed to enlighten the association between VAI and hsCRP in patients with PCOS.

In patients with PCOS, higher UA levels can be expected, as PCOS is considered a variant of MetS, and hyperuricemia is commonly coexisted with MetS. PCOS patients with IGT or IR have higher UA levels, compared to those without IGT or IR [48, 55]. On the other hand, there are studies reporting similar UA levels in PCOS patients, compared to controls [56, 57]. Laque-Ramirez et al. [57] reported that obese patients had higher UA levels than normal and overweight patients and that BMI was the main determinant of serum UA levels. In our study, UA levels were found to be higher in PCOS group, compared to BMI-matched controls. After we divided the groups into subgroups, only non-obese PCOS group was seen to have higher UA levels, compared to peer controls. In correlation analyses, UA levels were found to be correlated with WC, BMI, VAI, HOMA-IR, insulin and hsCRP in PCOS group, while correlated with WC, BMI and hsCRP levels in controls. In addition, VAI levels were also correlated with UA in all PCOS and overweight and/or obese PCOS groups. It is known that hyperandrogenemia can influence serum UA levels [58, 59] and hyperinsulinemia can decrease renal UA excretion [60]. Androulakis et al. [39] reported a positive correlation between VAI and UA levels in patients with PCOS. Although similar UA levels were determined in BMI-matched overweight and/or obese PCOS and overweight and/or obese controls, higher UA levels were found in all PCOS and non-obese PCOS groups, compared to peer controls, meaning that higher UA levels may be due to hyperandrogenism and IR in PCOS patients.

In our study, while SBP levels were similar, DBP were found higher in all PCOS, overweight and/or obese, and non-obese PCOS patients, compared to their peer controls. It is a known fact that the existence of systolic and/or diastolic hypertension is a frequently encountered entity in PCOS patients [2].

## Conclusion

In our study, VAI levels in PCOS patients were found at similar levels to those found in controls. However, when the participants were classified into subgroups according to their obesity scores, VAI levels were detected to be similar between non-obese PCOS and non-obese controls, while higher in overweight and/or obese PCOS patients than overweight and/or obese controls and non-obese PCOS. According to the formula of VAI, we found TG levels as the main determinant of VAI in patients with PCOS, compared to WC. In addition, we also determined that VAI levels were associated with some metabolic and inflammatory parameters such as HOMA-IR, UA and hsCRP. We consider that further studies with larger sample size are needed to enlighten the condition.

**Funding** This study was funded by the research fund of Konya Training and Research Hospital.

**Compliance with ethical standards**

**Conflicts of interest** Authors declare no conflicts of interest.

**Research involving human participants and/or animals** All procedures in the study involving human participants were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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