Study of Visceral and Subcutaneous Abdominal Fat Thickness and Its Correlation with Cardiometabolic Risk Factors and Hormonal Parameters in Polycystic Ovary Syndrome

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Abstract

Aim of the Study: This study aimed to compare the different adiposity parameters, namely visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) between patients with polycystic ovary syndrome (PCOS) and controls. In addition, it aimed to correlate these adiposity indices with hormonal parameters as well as cardiovascular (CV) risk factors in patients with PCOS. **Materials and Methods:** Newly diagnosed PCOS patients of reproductive age group according to Rotterdam criteria were included. Age- and body mass index (BMI)-matched healthy females with normal menstrual cycles were taken as controls. All the study participants underwent detailed clinical, biochemical, and hormonal evaluation. Transabdominal ultrasound (US) was performed for detailed ovary imaging and assessment of adiposity (SAT and VAT) parameters. **Results:** A total of 58 PCOS patients and 40 age- and BMI-matched controls were included. PCOS patients had significantly higher levels of androgens ($P < 0.001$), elevated highly sensitive C-reactive protein ($P = 0.007$), and higher degree of insulin resistance ($P < 0.001$) than controls. PCOS patients had a mean SAT of 2.37 ± 0.7 cm and mean VAT of 8.65 ± 1.78 cm. These parameters were significantly higher than controls who had a mean SAT of 2.01 ± 0.7 cm ($P = 0.014$) and mean VAT of 7.4 ± 1.89 cm ($P = 0.003$), despite both groups having similar BMI. Among PCOS cohort, VAT correlated positively with total testosterone ($r = 0.295$, $P = 0.025$) and negatively with dehydroepiandrosterone sulfate ($r = -0.210$, $P = 0.114$). However, no significant correlation was observed between SAT and androgens in PCOS group. **Conclusion:** PCOS patients, whether obese or nonobese, had elevated visceral adiposity than controls. VAT correlated positively with adverse CV risk factors and testosterone in PCOS patients. Hence, a simple and inexpensive ultrasonography screening of visceral fat may identify women who have adverse metabolic profile and enhanced CV risk.

Keywords: Androgen, highly sensitive C-reactive protein, insulin resistance, obesity, polycystic ovary syndrome, testosterone, visceral adipose tissue

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women. Due to its heterogeneity and uncertain etiology, PCOS is considered as a complex endocrine condition. Insulin resistance (IR) is a key feature relating to the metabolic dysfunction associated with PCOS.[1] Interestingly, premenopausal women with PCOS frequently present with central obesity, resulting from a masculinized body fat distribution consisting of deposition of energy surpluses in visceral adipose tissue (VAT) depots.[2] VAT is metabolically more active and has stronger association with dyslipidemia, hypertension, IR, glucose intolerance, and type-2 diabetes.[3] In women with PCOS, VAT independent of overall obesity plays a major role in the development of hyperandrogenism through IR and compensatory systemic hyperinsulinism.[4] Visceral adiposity in PCOS may induce premature atherosclerosis and increased cardiovascular (CV) mortality by mechanism that includes low-grade chronic inflammation, secretion of adipokines, and lipolytic activity, resulting in high rate of free fatty acid production.[5]

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In the past, studies have reported either increase[6-8] or no change[9,10] in subcutaneous adipose tissue (SAT) amount in PCOS patients. Similar conflicting data exist for VAT amount in PCOS which report either increase[6,7,11,12] or no change.[10] Data regarding these adiposity indices among Indian PCOS women are scarce. Hence, this cross-sectional, case–control study was undertaken to compare the adiposity parameters (VAT and SAT) between patients with PCOS and controls from our population. Furthermore, correlation of these adiposity markers with hormonal parameters as well as CV risk factors in patients with PCOS would also be assessed.

MATERIALS AND METHODS

The current study was undertaken in the department of endocrinology of a tertiary care center in eastern part of India from October 2015 to September 2016. A total of 58 female patients (15–45 years of age) newly diagnosed as PCOS according to Rotterdam criteria were included.[13] Forty age- and BMI-matched healthy females, with normal menstrual cycles and without clinical or biochemical evidence of hyperandrogenism, with normal ovary morphology on US, and with normoglycemia, were taken as controls. Exclusion criteria included menopausal women, those who have undergone hysterectomy or bilateral oophorectomy, pregnant and lactating women, and women with a previous history of hyperprolactinemia and thyroid disorders. All the study participants provided written informed consent. The study was approved by institutional ethical committee. All participants were asked to give a detailed menstrual history including age of menarche, regularity, duration, and number of cycles per year. Evidence of oligo-anovulation was provided by chronic oligomenorrhea, or by amenorrhea. Oligomenorrhea was defined as an intermenstrual interval of ≥35 days or a total of ≤9 menses per year and amenorrhea as absence of menstruation for >6 months. Clinical hyperandrogenism was defined by the presence of hirsutism (modified Ferriman–Gallwey score ≥8/36), persistence of acne in women older than 20 years, or the presence of androgenic alopecia. Specific etiologies were excluded by the finding of serum prolactin and thyrotropin levels within the normal range. Basal or cosyntropin-stimulated 17-hydroxyprogesterone levels (17OH-P) served to rule out nonclassic 21-hydroxylase deficiency. Clinical assessment served to rule out androgen-secreting tumors, Cushing's syndrome, and anabolic drug use.

All participants underwent detailed clinical examination. Body weight, height, waist and hip circumference, and blood pressure were measured as per standard protocol. BMI was calculated as the weight in kilogram divided by height in meters squared. For biochemical and hormonal measurements, overnight fasting blood samples were taken from each participant on the 2nd or 3rd day of their spontaneous or progesterone-induced menstrual cycles. Fasting plasma glucose was measured using an enzymatic colorimetric method with glucose oxidase. Lipid profile was also estimated. Serum fasting insulin level, Thyroid stimulating hormone (TSH), prolactin, dehydroepiandrosterone sulfate (DHEAS), testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were estimated using chemiluminescent microparticle immunoassay (CMIA) (Abbott Architect Plus i 2000 SR). 17OH-P was measured using radio immunoassay. Highly sensitive C-reactive protein (hsCRP) level was estimated using hsCRP kits (Siemens nephelometer BN™ II). A standard 75 g oral glucose tolerance test was performed to evaluate glucose tolerance status.

Trans-abdominal US was performed on the same day using a high-resolution B-mode Ultrasound System (Philips HD7) by a single experienced investigator. On the same sitting, adipose tissue depots were estimated. SAT thickness was defined as the depth from the cutaneous boundary to the linea alba and VAT was defined as the depth from the posterior surface of linea alba to the corpus of the lumbar vertebra.[14,15] The transducer was placed on the location where the xiphoid line intercepted the waist circumference. SAT was measured as the vertical distance from the skin to the linea alba with a 9L transducer (3–12 MHz) in the transverse position, and VAT as the vertical distance from the posterior surface of linea alba to the front edge of the vertebra with a 5C transducer (2–5 MHz) placed longitudinally. The image was captured during the expiratory phase of quiet respiration when the transducer was applied on the body surface without undue pressure. Both SAT and VAT were assessed twice and were calculated as the average of the two measurements.[14] Central obesity (waist circumference [WC] ≥80 cm) and obesity (BMI ≥25 kg/m^2) were defined by the National Cholesterol Education Program- Adult Treatment Panel (NCEP-ATP) III criteria. Metabolic syndrome (MetS) was defined according to the modified NCEP-ATP III criteria,[16] as the presence of any three of the following risk factors: (1) abdominal obesity defined by a WC of ≥80 cm; (2) fasting plasma glucose (FPG) of ≥100 mg/dl or drug treatment; (3) fasting triglyceride (TG) of >150 mg/dl in women or drug treatment; 4) fasting high-density lipoprotein (HDL)-cholesterol <50 mg/dl in women or drug treatment; (5) raised blood pressure defined as systolic blood pressure (SBP) of 130 mmHg, diastolic blood pressure (DBP) of >85 mmHg, or antihypertensive drug treatment. Homeostatic Model Assessment-Insulin Resistance (HOMA-IR) as a marker of IR was calculated as (FPG in mg/dl × fasting insulin in mU/L)/405.[17]

Statistical analysis
Descriptive statistical methods such as mean and standard deviation were applied to summarize continuous variables. Normality distribution of all parameters was checked using Shapiro–Wilk test. Mann–Whitney U-test and independent *t*-tests were performed to compare means between two groups having skewed and normal data distribution, respectively. Pearson's and Spearman's correlation coefficients were used to analyze correlation between normally distributed parameters and parameters with skewed distribution, respectively.

The data were analyzed using the IBM SPSS 24 statistical software (IBM Corp., Armonk, NY, USA).

RESULTS

The mean BMI of PCOS cases was 28.14 ± 5.94 kg/m² as compared to mean BMI of 27.0 ± 7.08 kg/m² among controls ($P = 0.39$). The clinical, biochemical, and hormonal variables of 58 PCOS patients and 40 controls are summarized in Table 1. When we compared the glycemic status (FPG and postglucose plasma glucose [PGPG]), lipid parameters (total cholesterol [TC], TG, HDL, and LDL), and blood pressure (SBP and DBP) among PCOS patients and controls, we did not find any significant difference ($P =$ nonsignificant for each parameter) [Table 1]. However, PCOS women had significantly higher levels of serum fasting insulin and HOMA-IR as compared to controls ($P < 0.001$ and $P = 0.001$, respectively). We found significantly elevated level of inflammatory marker (serum hsCRP) among PCOS women (5.76 ± 4.41 mg/L) as compared to controls (3.35 ± 3.14 mg/L) ($P = 0.007$). As expected, women

with PCOS had significant higher levels of androgens. The mean total testosterone and DHEAS among PCOS were significantly higher as compared to that of controls (283.43 ± 132.02 vs. 150.78 ± 64.47 µg/dl) ($P < 0.001$ for both). Similarly, LH levels were significantly higher among PCOS women in comparison to controls (6.37 ± 3.19 vs. 4.09 ± 1.91U/L) ($P < 0.001$).

Degree of adiposity was assessed by measurement of SAT and VAT with ultrasonography (USG) in cases and controls as described above. PCOS had significantly higher SAT (2.37 ± 0.7 cm) than controls (2.01 ± 0.7 cm) ($P = 0.014$). Similarly, VAT was also higher in PCOS (8.65 ± 1.78 cm) women in contrast to controls (7.4 ± 1.89 cm) ($P = 0.003$).

To study the influence of obesity on various hormonal and biochemical variables of PCOS patients, we divided the PCOS cohort into two groups based on their BMI. Group 1 (obese PCOS) had BMI ≥25 kg/m², whereas nonobese PCOS (BMI <25 kg/m²) comprised the second group. It was found that obese PCOS were relatively older

Table 1: Comparison of clinical, biochemical, and hormonal parameters among polycystic ovary syndrome patients and healthy controls

Parameters	PCOS group (*n*=58)	Control group (*n*=40)	*P*
Age (years)	21.86±5.22	22.72±5.11	0.42
BMI (kg/m²)	28.14±5.94	27.0±7.08	0.39
WC (cm)	92.04±12.86	89.22±15.03	0.208
WHR	0.91±0.07	0.92±0.08	0.22
SBP (mmHg)	119.86±14.66	117.65±12.81	0.545
DBP (mmHg)	77.27±8.84	77.8±7.92	0.76
FPG (mg/dl)	81.77±18.44	78.55±10.53	0.32
PGPG (mg/dl)	117±41.27	106.17±22.08	0.13
TC (mg/dl)	168.2±28.11	167.37±34.26	0.618
TG (mg/dl)	124.74±48.88	116.12±27.21	0.694
LDL (mg/dl)	100.36±24.34	101.07±26.48	0.831
HDL (mg/dl)	43.77±7.4	42.5±7.17	0.546
hsCRP (mg/L)	5.76±4.41	3.35±3.14	0.007
Fasting insulin (µIU/mL)	11.80±5.23	8.26±3.6	<0.001
HOMA-IR	2.4±1.28	1.62±0.79	0.001
LH (U/L)	6.37±3.19	4.09±1.91	<0.001
FSH (U/L)	5.26±2.25	4.4±1.47	0.057
Total testosterone (ng/dl)	55.36±31.92	25.35±10.48	<0.001
DHEAS (mcg/dl)	283.43±132.02	150.78±64.47	<0.001
SAT (cm)	2.37±0.7	2.01±0.7	0.014
VAT (cm)	8.65±1.78	7.4±1.89	0.003

Data are expressed as mean±SD. SD: Standard deviation, BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FPG: Fasting plasma glucose, PGPG: Postglucose plasma glucose, TC: Total cholesterol, TG: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, hsCRP: Highly sensitive C-reactive protein, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, DHEAS: Dehydroepiandrosterone sulfate, SAT: Subcutaneous adipose tissue, VAT: Visceral adipose tissue, PCOS: Polycystic ovary syndrome

Table 2: Comparison of clinical, biochemical, and hormonal parameters among obese polycystic ovary syndrome and nonobese polycystic ovary syndrome women

Parameters	Obese PCOS (*n*=38)	Nonobese PCOS (*n*=20)	*P*
Age (years)	23.05±5.75	19.6±3.03	0.01
BMI kg/m²)	31.06±5.13	22.58±2.23	<0.001
WC (cm)	98.35±10.46	86.05±7.22	<0.001
WHR	0.93±0.06	0.86±0.06	<0.001
SBP (mmHg)	124.1±14.13	111.8±12.31	0.001
DBP (mmHg)	80.0±8.18	72.1±7.82	0.001
FPG (mg/dl)	83.05±21.8	79.35±9.21	0.47
PGPG (mg/dl)	121±48.92	107.8±17.66	0.22
TC (mg/dl)	171.13±28.64	162.65±26.92	0.211
TG (mg/dl)	128.86±49.24	116.9±48.46	0.136
LDL (mg/dl)	101.57±25.33	98.05±22.79	0.572
HDL (mg/dl)	44.65±7.73	42.1±6.6	0.251
hsCRP (mg/L)	6.17±4.34	4.99±4.55	0.33
Fasting insulin (µIU/mL)	12.93±5.68	9.65±3.43	0.013
HOMA-IR	2.67±1.42	1.89±0.73	0.022
LH (U/L)	5.89±2.82	7.27±3.71	0.196
FSH (U/L)	5.07±2.04	5.61±2.63	0.689
Total testosterone (ng/dl)	59.95±35.73	46.64±21.17	0.133
DHEAS (mcg/dl)	271.32±129.95	306.45±136.22	0.34
SAT (cm)	2.63±0.68	1.87±0.38	<0.001
VAT (cm)	9.42±1.47	7.19±1.35	<0.001

Data are expressed as mean±SD. SD: Standard deviation, BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FPG: Fasting plasma glucose, PGPG: Postglucose plasma glucose, TC: Total cholesterol, TG: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, hsCRP: Highly sensitive C-reactive protein, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance, LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, DHEAS: Dehydroepiandrosterone sulfate, SAT: Subcutaneous adipose tissue, VAT: Visceral adipose tissue, PCOS: Polycystic ovary syndrome

than nonobese PCOS ($P = 0.01$) [Table 2]. Obese PCOS patients had significantly higher SBP and DBP than nonobese counterparts ($P = 0.001$). Fasting insulin level and HOMA-IR were significantly elevated in obese PCOS (12.93 ± 5.68 and 2.67 ± 1.42 µIU/ml) versus nonobese PCOS (9.65 ± 3.43 and 1.89 ± 0.73 µIU/ml), respectively ($P = 0.013$ and $P = 0.022$, respectively) [Table 2]. There was no significant difference between the two groups with regard to glycemic status (FPG and PGPG), lipid parameters (TC, TG, LDL, and HDL), and inflammatory marker hsCRP ($P =$ nonsignificant for each interaction) [Table 2]. When comparison of the hormonal parameters among obese PCOS and nonobese PCOS was done, no significant difference between the two groups with regard to FSH and LH was found ($P = 0.689$ and $P = 0.196$, respectively). Similarly, we did not find any significant difference in mean total testosterone and DHEAS level among obese PCOS and nonobese PCOS ($P = 0.133$ and $P = 0.34$, respectively) cohort. As expected, obese PCOS patients had significantly higher SAT and VAT in comparison to nonobese PCOS controls ($P < 0.001$ and $P < 0.001$, respectively).

To assess status of adiposity indices (VAT and SAT) and metabolic parameters among cases and controls when BMI was matched, we divided PCOS and control group into obese and nonobese subgroups, respectively. First, we compared parameters between obese PCOS and obese control group, respectively. The two groups were similar with regard to age, BMI, WHR, glycemic status, lipid parameters, and hsCRP ($P =$ nonsignificant for each parameter [Table 3]. However, two interesting results also emerged. First, the obese PCOS group had significantly elevated fasting insulin and

HOMA-IR despite having similar BMI to that of control group. Second, the former group also had significantly higher SAT and VAT even if their BMI and WHR were similar [Table 3].

Similar to the above assessment, we compared the metabolic and adiposity parameters between nonobese PCOS and nonobese controls. It was observed that BMI, WHR, and lipid parameters were comparable between these two groups. The nonobese PCOS group had adverse CV risk factors such as elevated FPG ($P = 0.04$) and hsCRP ($P = 0.04$) but not PGPG ($P = 0.08$) than nonobese controls [Table 3]. We also found that nonobese PCOS group had significantly elevated fasting insulin and HOMA-IR, a trend which was also observed for obese PCOS patients. These findings reflect the insulin-resistant state inherent to PCOS patients despite comparable BMI. A dichotomy was observed for adiposity indices in the nonobese cohort. Only VAT (but not SAT) was higher among nonobese PCOS group ($P < 0.01$) in comparison to nonobese controls [Table 3]. Hence, our results suggest that visceral obesity is high even in nonobese PCOS which may contribute to adverse CV profile.

We also assessed the correlation of SAT and VAT with various clinical, metabolic, and hormonal parameters. Among PCOS group, SAT correlated positively and significantly with VAT ($r = 0.547$, $P < 0.001$), WC ($r = 0.568$, $P < 0.001$), WHR ($r = 0.325$, $P = 0.013$), BMI ($r = 0.534$, $P < 0.001$), and DBP ($r = 0.282$, $P = 0.032$). Other parameters such as lipid profile, SBP, HOMA-IR, total testosterone, and DHEAS did not show significant correlation with SAT ($P =$ nonsignificant for each parameter). Similarly, VAT also correlated positively and

Table 3: Comparison of clinical, biochemical, and hormonal parameters among obese polycystic ovary syndrome versus obese controls and nonobese polycystic ovary syndrome versus nonobese controls

Parameters	Obese PCOS women (n=38)	Obese controls (n=23)	P	Nonobese PCOS women (n=20)	Nonobese controls (n=17)	P
Age (years)	23.05±5.75	22.3±5.58	0.621	19.6±3.03	23.29±4.51	0.005
BMI (kg/m²)	31.06±5.13	31.41±6.03	0.812	22.58±2.23	21.02±2.53	0.055
WC (cm)	98.35±10.46	98.21±12.52	0.749	80.05±7.22	77.05±7.85	0.27
WHR	0.93±0.06	0.95±0.08	0.408	0.86±0.06	0.9±0.06	0.085
SBP (mmHg)	124.1±14.13	123.91±10.99	0.646	111.8±12.31	109.17±10.07	0.357
DBP (mmHg)	80.0±8.18	80.6±7.37	0.771	72.1±7.82	74.0±7.17	0.45
FPG (mg/dl)	83.05±21.8	81.91±12.24	0.82	79.35±9.21	74.0±5.11	0.04
PGPG (mg/dl)	121±48.92	111.56±26.56	0.358	107.8±17.66	98.88±10.96	0.08
TC (mg/dl)	171.13±28.64	169.52±31.31	0.639	162.65±26.92	164.47±38.69	0.988
TG (mg/dl)	128.86±49.24	122.87±26.69	0.982	116.9±48.46	107.0±25.89	0.707
LDL (mg/dl)	101.57±25.33	99.3±22.33	0.666	98.05±22.79	103.47±31.82	0.798
HDL (mg/dl)	44.65±7.73	43.69±6.98	0.715	42.1±6.6	40.88±7.31	0.707
hsCRP (mg/L)	6.17±4.34	4.46±3.12	0.105	4.99±4.55	2.27±2.79	0.04
Fasting insulin (µIU/mL)	12.93±5.68	9.03±3.8	0.006	9.65±3.43	7.23±3.12	0.033
HOMA-IR	2.67±1.42	1.84±0.86	0.017	1.89±0.73	1.32±0.59	0.012
SAT (cm)	2.63±0.68	2.22±0.76	0.047	1.87±0.38	1.72±0.49	0.424
VAT (cm)	9.42±1.47	8.57±1.35	0.037	7.19±1.35	5.83±1.27	0.003

Data are expressed as mean±SD. SD: Standard deviation, BMI: Body mass index, WC: Waist circumference, WHR: Waist hip ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FPG: Fasting plasma glucose, PGPG: Postglucose plasma glucose, TC: Total cholesterol, TG: Triglyceride, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, hsCRP: Highly sensitive C-reactive protein, HOMA-IR: Homeostatic Model Assessment of Insulin Resistance, SAT: Subcutaneous adipose tissue, VAT: Visceral adipose tissue, PCOS: Polycystic ovary syndrome

significantly with WHR ($r = 0.489$, $P < 0.001$), BMI ($r = 0.656$, $P < 0.001$), SBP ($r = 0.426$, $P = 0.001$), and DBP ($r = 0.374$, $P = 0.004$). However, no significant correlation was noted for glycemic parameters, lipid parameters, and markers of IR with VAT. Interestingly, VAT correlated positively with total testosterone ($r = 0.295$, $P = 0.025$) and negatively with DHEAS ($r = -0.210$, $P = 0.114$).

DISCUSSION

In this study, we demonstrated that our PCOS patients had higher abdominal SAT than healthy controls. Similar to our study, Karabulut *et al.* had also found increased SAT amount in PCOS in comparison to controls.[8] In our study, it was also observed that SAT amount was higher in obese PCOS in contrast to obese controls despite similar BMI in these two groups. Some previous studies have also reported increased abdominal subcutaneous fat amount in overweight PCOS patients.[6,7] However, we did not find any significant difference of SAT amount among nonobese PCOS and nonobese controls. In agreement to our results, Yildirim *et al.* also did not find a difference in SAT between the lean PCOS and healthy groups.[18] US is a noninvasive, inexpensive, nonionizing, validated, and accessible method for measuring abdominal fat compartments in epidemiological studies.[14,19-21] US has been successfully used to assess VAT and SAT in various previous studies and can be useful in women with PCOS.[22,23] Visceral fat thickness assessed by USG highly correlates with measurements made with computed tomography (CT) or magnetic resonance imaging (MRI).[24,25]

It is unclear whether abdominal subcutaneous fat tissue is associated with CV risk factors.[26] To look for this association, we used correlation analysis of SAT with various CV risk factors. We found a positive correlation of SAT with BMI, WC, WHR, DBP, and fasting insulin. Two studies have explored the association of SAT with CV risk factors and IR. One reported positive correlation of SAT with IR and dyslipidemia.[27] In contrast to it, another showed that subcutaneous fat mass was not associated with metabolic variables including IR and dyslipidemia in PCOS.[28]

In the present study, we found significantly higher VAT thickness in women with PCOS than controls. This confirms that visceral adiposity is increased in PCOS as VAT reflects visceral adiposity. Borruel *et al.* evaluated US measurements of adipose tissue depots including subcutaneous, preperitoneal, mesenteric, epicardial, perirenal fat thicknesses, and total body fat mass in patients with PCOS.[27] They found that both obese and nonobese women with PCOS have increased amount of VAT, especially in the intraperitoneal and mesenteric depots.[27] Consistent with the results of Borruel *et al.*, we also noted higher VAT amount in obese PCOS and nonobese PCOS women when they were compared with obese controls and nonobese controls, respectively. Conflicting data exist in the literature regarding the role of BMI on body fat distribution in PCOS. Few studies showed that overweight PCOS females had more visceral fat

than overweight controls.[6,7,12] While some studies found no differences in body fat distribution between lean PCOS patients and lean controls, other studies reported that lean PCOS patients showed a significantly higher visceral fat mass than controls.[11,18,29] In our study, we also found that nonobese PCOS women had significantly higher VAT in comparison to nonobese controls. Hence, it may be opined that PCOS patients have higher visceral adiposity irrespective of their BMI.

In our study, VAT correlated significantly with CV risk factors such as central obesity (WC and WHR), BMI, and blood pressure. Hence, VAT may be an independent predictor of CV risk among women with PCOS. Visceral fat has a strong association with CV risk factors, particularly dyslipidemia and hyperinsulinemia.[3] In PCOS, this association has been shown in a number of studies.[6,8,18,27] However, in contrast to this, we did not find any significant correlation of VAT with FPG, hyperinsulinemia, and dyslipidemia among our PCOS patients.

We found a positive correlation of VAT with serum testosterone suggesting the role of this sex steroid in masculinized body fat deposition in the abdominal VAT depots of women with PCOS. In agreement to our findings, few studies have shown that intra-abdominal fat or VAT correlates positively with testosterone level in PCOS women.[30] VAT may contribute to hyperandrogenemia in PCOS either by increasing the degree of IR or by increasing obesity that predispose these women to metabolic dysfunction and CV risk. In our study, VAT showed an inverse correlation with DHEAS suggesting the metabolically beneficial role of this adrenal androgen, though the association was not statistically significant. Brennan *et al.* found an independent association of high DHEAS levels with decreased IR in a cohort of 352 women with PCOS.[31] The increased DHEAS level seen in PCOS is mainly as a result of hyperinsulinemia. The role of this adrenal androgen in metabolic disturbance in women with PCOS is still unclear.

PCOS women in our cohort had significantly higher hsCRP (a surrogate marker for degree of inflammation) than controls. Similar to our study, Ramanand *et al.* also found higher hsCRP level among their PCOS women.[32] Although obesity is a major factor associated with inflammation in individuals with MetS, the visceral fat independent of total adiposity plays a major role.[33,34] Since PCOS is associated with central obesity, this would explain why inflammation is seen in this syndrome. In agreement to the above statement, we also found that our PCOS women had both elevated hsCRP and VAT than controls. Further subgroup analysis revealed that hsCRP levels are similar among obese PCOS and obese controls. This possibly indicates that BMI could be an important determinant of hsCRP (inflammatory marker). However, despite having similar BMI like nonobese controls, nonobese PCOS individuals have increased visceral adiposity (VAT) and subclinical inflammation (hsCRP), which further reinforces the interaction of visceral adiposity and inflammation in PCOS.

Our study has few limitations. First, our sample size is relatively small and hence results cannot be generalized. Second, we

have assessed only one marker (hsCRP) to assess subclinical inflammation. Third, we have only used USG-measured VAT and SAT for adipose tissue quantification. Methods such as CT, DEXA, or MRI provide more robust results than USG. However, we have used USG as it is easily available, noninvasive, and inexpensive, and moreover the USG-derived values correlate well with other established methods. Another advantage is that VAT and SAT estimation can be done during same time when routine USG is undertaken for PCOS.

Conclusion

Hence, women with PCOS (both obese and nonobese) have elevated visceral adiposity than controls. Despite having normal BMI, nonobese PCOS women have elevated visceral adiposity and elevated inflammatory marker than nonobese controls. Furthermore, VAT correlated positively with adverse CV risk factors and testosterone in PCOS women, which further reinforces the association of visceral adiposity with adverse CV profile and hyperandrogenemia characteristic of PCOS. Hence, a simple and inexpensive USG screening of visceral fat may identify women who have adverse metabolic profile and enhanced CV risk.

Conflicts of interest

There are no conflicts of interest.

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