Value of visceral fat assessment in identifying metabolic syndrome in overweight females with polycystic ovary syndrome (PCOS)

Abstract

Objective. *The study assesses the usefulness of a new method of calculating the visceral fat in identifying metabolic syndrome (MetS) in overweight females diagnosed with polycystic ovary syndrome (PCOS).* ***Study Design.*** *Prospective diagnostic study. Study group: 49 overweight females with PCOS (Rotterdam 2003 diagnostic criteria), and 99 without PCOS as controls, recruitment period: 09.2008 - 03.2010. Body composition analysis: segmental bioimpedance assessment. Morphometric and biological parameters were measured. The assessed visceral fat was used as a new screening tool for MetS in overweight patients with PCOS.* ***Statistical analysis.*** *descriptive analysis, equal variance T test, Receiver operating curve for diagnostic value assessment.* ***Results.*** *MetS incidence: 26.53% of PCOS cases and 19.59% in controls. Estimating visceral fat has a good sensitivity (79.31%) and specificity (70.34%) in identifying MetS, with 7 as diagnostic threshold.* ***Conclusion.*** *Monitoring visceral fat can identity cases with MetS in PCOS patients without any further invasive approach.*

Keywords: *visceral fat, overweight, polycystic ovary syndrome, metabolic syndrome*

Dana Stoian[1,2], Dan Bogdan Navolan[1]

1. Department of Obstetrics and Gynecology, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania
2. Clinic Dr. D , Timisoara, Romania

Correspondence: Dr. Dana Stoian
e-mail: drd@nutritietimisoara.ro

The work was partialy granted by POS CCE Nr. 202/15.07.2010

Introduction

The polycystic ovary syndrome (PCOS) is the most common endocrine disorder that affects the female population of reproductive age. PCOS incidence is variable, ranging from 4%[(1)], 7.1%[(2)] to 33%[(3)], depending on the working group, ethnic group(4, 5) or definition criteria for metabolic syndrome[(3)]. There are many diagnostic criteria; generally the presence of oligo- or anovulation, the clinical and/or biochemical signs of hyperandrogenism are considered, excluding other diseases: Cushing's syndrome, 21 hydroxylase deficiency, other forms of congenital adrenal hyperplasia, hypothyroidism, androgen secreting tumors[(4,5)]. Highlighting the morphology of the polycystic type is not compulsory; on the contrary, 8-25% of healthy women and 14% of those under contraceptive therapy show the typical ultrasound appearance[(6)]. Overweight and peripheral insulin resistance is common issues encountered in this syndrome[(2)]. Obesity and insulin resistance are closely linked to the initiation and maintenance of hyperandrogenemia[(2,7)]. Obesity, especially the abdominal one, may play a pathogenic role in the development of PCOS[(8)] favoring excess androgen synthesis. Hyperandrogenemia *per se* favors visceral obesity[(9)] in its turn.

The core of PCOS is the metabolic syndrome and the metabolic risk. This is the difference between simple ovarian cysts and PCOS, respectively the metabolic implication, cardiovascular and diabetic long-term risk, for this particular group of young females. The severity of the metabolic impairment differs in overweight females with PCOS, the implications regarding cardiovascular risk being more important than we think. Assessing visceral fat seems the logic intermediate step in evaluating MetS presence in PCOS cases[(10)], trunk fat being a good predictor of metabolic changes[(11)].

Segmental bio impedance has a demonstrated excellent agreement with DEXA body composition assessment[(12)], including trunk fat. TANITA Company developed recently in 2010 new software that evaluates visceral fat by calculation or by measurement of segmental body composition with eight electrodes[(13)].

Our study aims to evaluate for the first time mainly the possible use of trunk fat measurement and visceral fat assessment, with new developed software in overweight PCOS cases in identifying the presence of coexisting metabolic syndrome.

Methods

The study group was recruited from patients who resorted of the Department of Obstetrics and Gynecology of the Victor Babes University of Medicine and Pharmacy in Timisoara, and the Clinic Dr. D, in the endocrine ambulatory, between September 2008 and March 2010. All the cases were self-addressed for esta-

Received: *March 30, 2012*
Revised: *May 07, 2012*
Accepted: *June 09, 2012*

blishing a weight loss program by our endocrinologist, because of her results in the field of weight loss and life style changes. All the patients entitled themselves as "healthy but overweight". Data were partially stored in Astraia Software, the gynecology module (www.astraia.de - Astraia GmbH, Munchen, Germany).

Out of the total of 227 women who came for assessment in order to establish a nutrition program we identified 49 cases with PCOS, 20 cases were of normal weight (Body mass index BMI lower than 25), 59 subjects met one of the exclusion criteria, and 99 cases formed our control group - overweight without PCOS. Their age was between 16 and 40, the mean age being 29.35±6.225, their weight was between 54 and 124.9 kg, the mean weight being 90.76±15.24 kg, median WEIGHT OF 88.75 KG, and their body mass index (BMI) was 31.50±5.18 kg/m^2, ranging between 25.4 and 46.9 kg/m^2.

■ **Inclusion criteria:** Young females address by themselves to the endocrine unit of our clinic, starting September 2008 to March 2009, with weight exceeding the ideal weight for one's age (BMI>25 kg/m^2), age below 40, with not known endocrine disease.

■ **Exclusion criteria:** hypothyroidism (37), 21-hydroxylase deficiency (5 non-classical form/late-onset), primary hypercortisolemia (one case), functional hyperprolactinemia (15 cases), precocious ovarian failure - premature menopause (0 cases), diabetes mellitus, hypertension, normal weight (BMI < 25 kg/m^2) and morbid obesity (BMI>45 kg/m^2).

All patients completed a comprehensive assessment protocol:

■ **Anthropometric assessment:** height (without shoes) by means of a stadiometer (Tanita Corp. Japan), weight (without clothes), BMI calculation. Abdominal circumference was measured with a tape 1 cm wide, as the minimum circumference between the iliac crest and rib side edges, respectively hip circumference as the maximum circumference of the hips.

Body composition was determined by means of an analyzer of electrical bioimpedance, device: Tanita BC-418, Tanita Corp. Japan, with evaluation of composition of each segment and determining the basal metabolic rate (BMR). The general and segmental composition of trunk, upper and lower limbs was assessed for each patient. Visceral fat assessment was performed by calculation by the TANITA software (upgrade version 2011)[13];

■ **Assessment of menstrual disorders:** cycle length, inter-menstrual bleeding, and menstrual flow changes;

■ **Hirsutism:** we considered in cases with Ferriman Gallwey score 8. The scale is used for hirsutism evaluation, a self-assessment of facial hair, trunk hair, pubic hair, respectively arms and leg hair appearance. Normal values are below 6, normal body hair with abnormal distribution: values 6-8, excessive pilosity for values over 8;

■ **Metabolic Assessment:** determining blood glucose, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (Tg), glycated hemoglobin, uric acid;

■ **Hormonal profile:** free testosterone, 5-dehydroepiandrosterone sulphate, androstenedione, luteinizing hormone/follicle stimulating hormone ratio, 17 hydroxyprogesterone, thyroide stimulating hormone, prolactin, plasma cortisol.

■ **Diagnostic criteria used:**

1. Hypothyroidism: thyroid stimulating hormone greater than 4 IU/mL, with or without symptoms or obvious clinical signs;

2. Primary hypercorticism: elevated plasma cortisol values, insuppressible with nocturnal inhibition with 1 mg dexamethasone;

3. 21-hydroxylase deficiency: increased levels of 17-hydroxyprogesterone, positive response to stimulation with 100 mg adrenocorticotropic hormone;

4.PCOS Definition by Rotterdam 2003 criteria: anovulation/menstrual disorders, hyperandrogenemia: Ferriman-Gallwey score over 8, elevated free testosterone values >0.011 nM/L, 5-dehydroepiandrosterone sulphate above the age appropriate limit, polycystic ovary morphology in ultrasound images;

5. MetS (at least three criteria): waist circumference ≥80 cm, hypertension ≥130/85 mmHg or antihypertensive therapy, hypertriglyceridaemia, Tg ≥150 mg/dL, hypercholesterolemia, HDL-C <50 mg/dL

Objective

Considering that visceral fat is the key point that initiates metabolic impairment in overweight people, and women with PCOS are at a higher metabolic risk, we wanted to evaluate the value of visceral fat in predict de presence of MetS in PCOS overweight women. Metabolic evaluation is recommended, but usually this patients address to the gynecologist office for menstrual cycle alteration or infertility and usually are not compliant to metabolic evaluation. Developing a screening tool, noninvasive, rapid, reproducible that could identify the MetS group among these cases should be of great help for our gynecological-endocrinological practice.

Statistical Analysis

Evaluation of means, paired T test, receiver operating curve (ROC) diagnostic test with calculation of sensitivity, specificity, negative predictive value, positive predictive value were performed with the NCSS 2007 software. The diagnostic value was assessed by Area under ROC (AUC).

Results

a. Study group characteristics and metabolic imbalances in overweight patients with PCOS compared with controls. The prevalence of MetS in the entire study group is (case with and without PCOS) 19.59%. As expected, there was a significant differences between the prevalence of MetS in the

group of the overweight patients without PCOS (16 out of 99 cases, 16.16%) anin overweight PCOS cases (13 out of 49 cases 26.53%, p<0.01).

The mean weight and body mass index (BMI) of patients who have PCOS are higher as compared to that of patients without PCOS, but does not reach the threshold of statistical significance. The difference is emphasized when body composition is assessed, the adipose tissue being significantly better represented in the case of PCOS. The percent of total body fat is significantly higher in the PCOS group (38.22±7.20 %) than in controls (36.31±5.65 %), p<0.06. Also trunk fat and visceral fat are significantly higher in PCOS cases as compared to controls (Figure 1).

Differences between the two groups are apparent not only in morphometry, body composition and degree of obesity but also from the metabolic point of view. But the presence of MetS makes a difference.

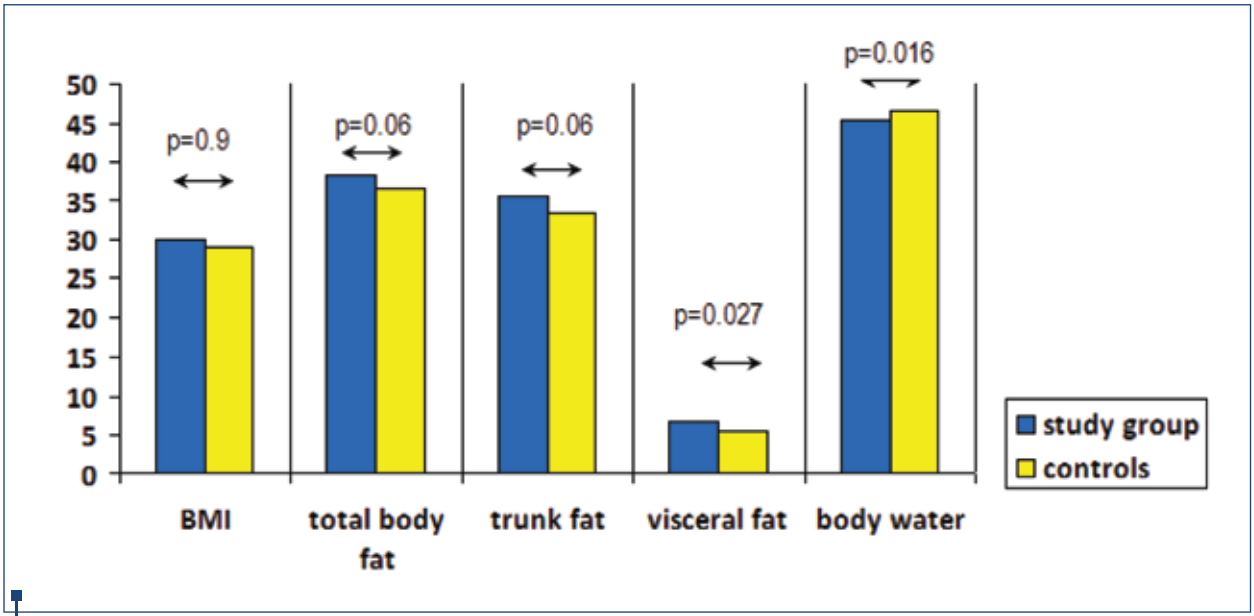

Figure 1. Body composition in overweight patients with PCOS compared with controls. The mean was represented (on the ordinate) for the two groups of patients, compared with the paired T test

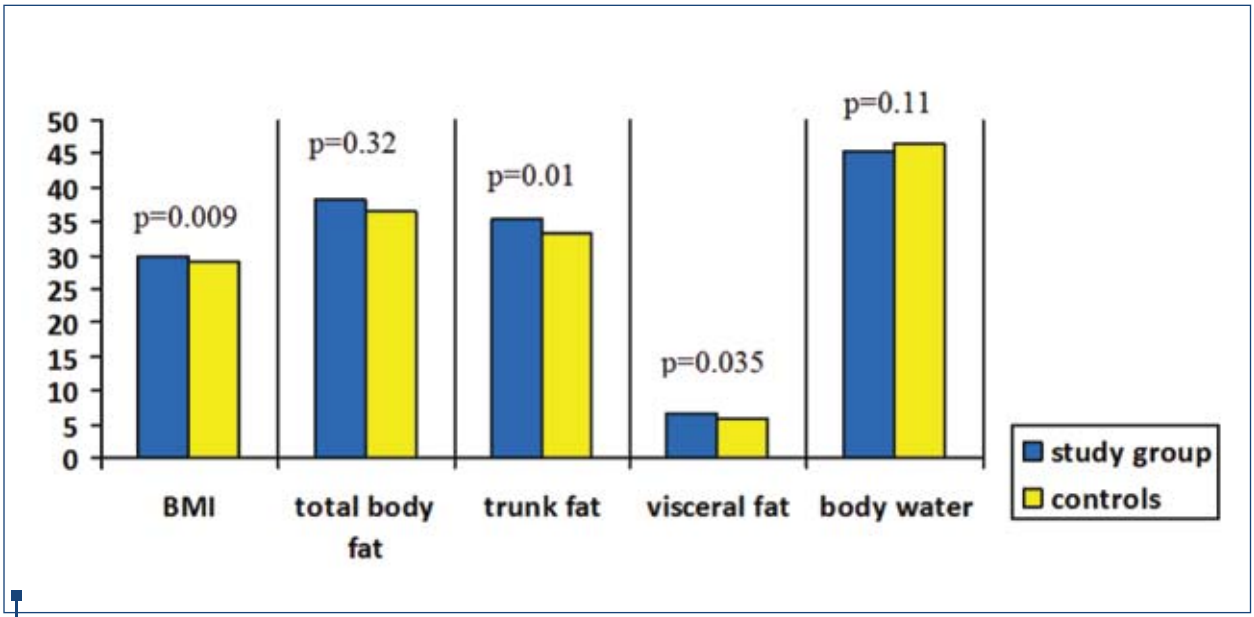

Figure 2. Differences between metabolic parameters in patients with PCOS compared with controls. The mean was represented (on the ordinate) for the two groups of patients, compared with the paired T test

Table 1 Antropometric/body composition assessment in overweight patients with and without PCOS

	Overweight patients		p
	without PCOS	with PCOS	
No of cases	99	49	
Age (years)	29.88±6.46	28.41±5.33	0.172
High (cm)	165.07±9.30	164.02±5.96	0.475
Weight (kg)	79.53±14.21	84.26±16.47	0.037
BMI (kg/msc)	28.9±4.97	31.00±5,35	0.010
Waist (cm)	108.5±14.5	110.2±10.4	0.7
Hip (cm)	115±10.2	116.4±8.9	0.8
Total body fat (%)	36.81±6.36	38.22±7.2	0.04
Trunk fat (%)	33.38±6.39	35.44±8.01	0.02
Visceral fat	7.05±2.65	7.68±3.06	0.01

Table 2 Antropometric/body composition assessment in PCOS cases versus controls with and without MetS

	Controls (n=99)		PCOS cases (n=49)	
	No MetS	+ MetS	No MetS	+ MetS
No of cases	83	16	36	13
Age (years)	31.17±6.04	29.62±6.5	28.83±3.24	28.27±5.9
Height (cm)	165. 05 ± 9.9	165.117±4.98	164.33±5.83	163.08±6.86
Weight (kg)	78.41±13.99	84.93±14.47	82.7±16.33	88.96±17.28
BMI (kg.msc)	28.46±5.06	31.00±3,98	30.16±5.028	33.43±5,76
Weist (cm)	98.25±6.6	100.2±6.7	99.6±7.8	101.4±6.8
Hip (cm)	108.4±7.9	110.5±9.7	110.3±3.4	114.4±10.2
Total body fat (%)	35.99±5.76	38.51±4.32	37.06±6.82	41.69±7.50
Body water (%)	46.88±4.19	45.35±3.12	46.26±4.58	42.99±5.75
Glicemia (mg/dL)	89.20±12.51	93.66±12.36	93.5±10.79	99.83±11.8
HDL-C (mg/dL)	51.09±9.28	47.94±6.31	51.48±14.19	43.76±5.87
LDL-C (mg/dL)	125.13±21.94	146.04±6.31	125.02±20.60	159.66±25.81
Tg (mg/dL)	125.65±27.60	172.95±20.41	136.25±31.83	177.91±22.58
Hb A1c (%)	5.45±0.65	5.40±0.97	5.75±0.62	6.1±0.64
Uric acid (mg/dL)	4.30±1,156	3,61± 1.20	4,37±1.40	4,76±1.33

Patients with PCOS have significant higher values of glycated hemoglobin (p=0.035), glicemia (p=0.009) and Tg (p=0.029), LDL-C (p=0.01) compared with controls. The other metabolic parameters, HDL-C and uric acid were higher in PCOS group, even though the differences did not met a level of significance (p=0.32, p=0.11) (Figure 2)

b. MetS PCOS cases: a distinct category in the study group: Morphometric/anthropometric and metabolic characteristics

The mean Weight, BMI, Weist and Hip size of patients wit MetS is higher as compared to that of patients without MetS in both groups: with or without PCOS. The difference is emphasized when body composition is assessed, the adipose tissue being significantly better represented in the patients with MetS. The overweight patients in the presence of PCOS have a higher total fat, trunk fat and visceral fat as compared with controls (Table 2).

Differences between the two groups are apparent not only in morphometry, body composition and degree of obesity but also from the metabolic point of view.

In both groups of overweight females, with or without PCOS, cases with MetS have significant higher values of glycaemia, Tg and LDL-C compared with cases without MetS in both groups (with or without PCOS) (Table 2).

The metabolic assessment of the two groups of patients shows a high incidence of metabolic complications in the MetS group. Each metabolic component is modified to a greater extent in cases with PCOS and MetS.

c. Visceral fat analysis in prediction metabolic syndrome: Receiver Operator Curve (ROC)

Each performed calculation assessed the visceral fat. Although values over 13 are considered high[13], we observed mean higher values of visceral fat in PCOS cases compared with controls (Figure 1) but also there was a significant difference between PCOS cases also (TABLE III): in the presence of MetS, visceral fat is higher as compared with PCOS cases without MetS (T = -3.7964, p=0.0001). We observed the same tendency of body distribution in control cases, but the significance level was not achieved (T = -1.864, p=0.03). The difference is also observed between PCOS MetS cases compared with control MetS cases (T=-0.3272, p=0.0047) - Table 3.

Table 3 Body composition measurements in PCOS cases compared with controls

	Controls		PCOS cases	
	No MetS	+ MetS	No MetS	+ MetS
Total fat (%)	35.99±5.76	38.51±4.32	37.06±6.82	41.69±7.50
Trunk fat (%)	32.9±6.63	34.96±5.46	34.60±7.48	38.03±10.2
Perivisceral fat	5.24±2.54	7.76±2.22	6.22±2.97	8.08±3.08

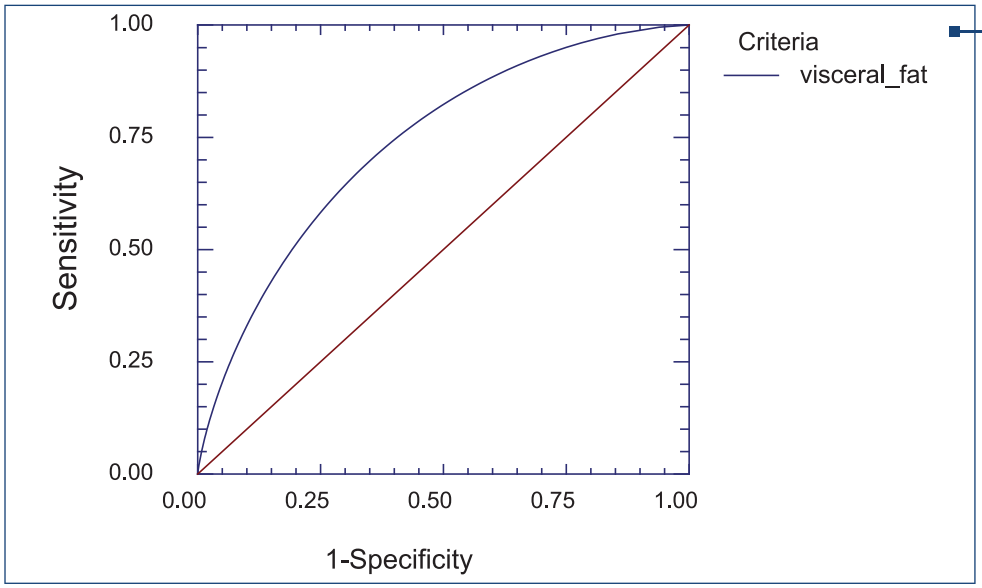

Figure 3. Receiver operator curve for the visceral fat value in MeTS diagnostic in cases with PCOS

Table 4 Sensitivity, specificity, PPV and NPV for visceral fat values in diagnostic of MetS

Visceral fat cutoff value	Sensitivity	Specificity	Like hood ratio	PPV	NPV
1	1.00	0.000	1.00	0.197	1.000
2	1.00	0.016	1.017	0.200	1.000
3	0.965	0.084	1.054	0.205	0.909
4	0.931	0.228	1.207	0.228	0.931
5	0.896	0.381	1.449	0.262	0.937
6	0.827	0.584	1.992	0.328	0.932
7	0.793	0.703	2.673	0.396	0.932
8	0.517	0.830	3.051	0.428	0.875
9	0.448	0.872	3.526	0.464	0.865
10	0.344	0.915	4.068	0.500	0.850
11	0.103	0.940	1.743	0.300	0.810
13	0.034	0.957	0.813	0.1667	0.801
15	0.000	0.991	0.000	0.00	0.801

We analyzed the value of the visceral fat monitoring in identifying MetS with the receiver operator curve. The area under curve (AUC) defines a high diagnostic value of the test: AUC = 79.301% (p=0.0007) (Figure 3).

We defined the threshold value for the studied parameter (visceral fat) as 7, having the best sensitivity (79.31%) and specificity (70.339%) selected from all parameter values - Table 4.

The same threshold value has a positive predictive value (PPV) of 39.6%, respectively a very high negative predictive value of 90.05%.

Discussion

The purpose of this study was to evaluate the possibility of MetS risk stratification by assessing body composition details, respectively visceral fat. We defined a control group made up by patients whose weight was over the ideal weight for their age, who did not meet the diagnostic criteria of ovarian involvement of the hyper androgenic type. Under the same conditions of height, weight, age and BMI, the prevalence of metabolic involvement is much higher in subjects with PCOS.

The relatively high prevalence (25.6%) of MetS falls within the limits described in literature[14,15]. But there are studies that show a lower incidence of only 5 to 10%[16]. Yet diagnostic criteria of MetS often vary, low-prevalence studies[16] have the same incidence of about 20% (22.7%) when there are two metabolic changes and also an increased waist circumference. Even without the criteria for MetS, the prevalence of metabolic problems was high (50-55%), as described in the literature[4]. Also the use of adult, respectively adolescent criteria generates differences[14]. We can consider that the presence of PCOS increases the prevalence of MetS[14,15,16]. In our case the estimated RR of

MetS in the presence of PCOS was four times higher, similarly to other studies[15].

As we saw from the data of Table II, not only the prevalence but also the severity of metabolic imbalance are higher in cases of associated PCOS: basic hyperglycemia as well as hypertriglyceridemia are significantly higher[15,16].

Increased visceral fat determines a higher metabolic risk, independent of weight excess[17]. Regional distribution of fat is considered a better predictor of BMI in metabolic risk[18,19,20].

Data regarding monitoring metabolic risk in PCOS cases are few. A study similar to our was conducted in 30 cases diagnosed with PCOS, but this evaluated metabolic risk as compared with trunk fat, not with abdominal visceral fat[10]. Even so, they did observe a link between altered metabolic parameters and fat. Another study followed body composition changes in 10 PCSO cases, but with no direct referral to metabolic risk highlighting differences in visceral fat as compared to controls[21]. We also observed a more severe visceral fat deposition as compared with controls ($p = 0.0001$). Similar results with our study were observed when the visceral fat was indirectly assed by measuring peri-hepatic fat deposition in 114 cases with PCOS[22].

Our study identified also our own optimum visceral fat threshold in identifying with the best diagnostic power the risk of MetS with a validated body composition analysis method[13].

The objective of our study is evolving in the general trend of identifying screening tools for risk stratification that are noninvasive, reproducible, easy to perform, with low cost and no side effects[23].

To our knowledge, this is the first study, which overweight assessment includes measuring of the presence and distribution of adipose tissue (visceral fat) by determining electrical bio impedance of tissues. Higher abdominal fat content are associated with the presence of PCOS and MetS as compared with control group, as abdominal fat and obesity related hyperinsulinemia favors hyperandrogenism[9]. Assessing visceral fat by measuring electrical bio impedance measurement has all the above mentioned characteristics.

Conclusions

1. PCOS is associated with high incidence of MetS as compared with aged matched controls.

2. The severity of metabolic imbalance (assessed by percent of changes and also degree of variance from the upper normal range) is more important in overweight PCOS cases, as compared with overweight age matched controls.

3. In the same age group and weight excess, there are significant body composition differences between overweight females with PCOS as compared with patients without PCOS diagnostic criteria. There are significant differences in the respect of total fat/trunk fat and especially visceral fat.

4. Monitoring visceral fat identifies the PCOS cases with metabolic syndrome. Our identified visceral fat threshold was 7. Diagnostic power of visceral fat assessment in MetS diagnostic is good, with an AUC of over 90%.

5. Measuring visceral fat by segmental electric bio impedance measurement can be a good non-invasive-screening tool for metabolic syndrome in PCOS cases. ■

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