European Journal of Obstetrics & Gynecology and Reproductive Biology 192 (2015) 66–71

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Obesity and inflammatory biomarkers in women with polycystic ovary syndrome

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ARTICLE INFO

Article history:
Received 1 July 2014
Received in revised form 13 June 2015
Accepted 24 June 2015

Keywords:
Adiponectin
Leptin
Resistin
Obesity
Inflammation
PCOS

ABSTRACT

Objective: To evaluate the roles of obesity and inflammatory biomarkers associated with medical complications in women with PCOS.
Study design: Retrospective, BMI-matched study. A total of 330 patients, including 165 women with PCOS and 165 women without PCOS, were evaluated. The insulin resistance (homeostasis model assessment insulin resistance index – HOMA) and lipid profiles were assessed. The adiponectin, leptin, ghrelin, resistin, anti-müllerian hormone (AMH), sex hormone-binding globulin (SHBG), high sensitivity C-reactive protein (hs-CRP), and interleukin-6 (IL-6) levels were also measured.
Results: Women with PCOS had significantly higher AMH, fasting insulin, total cholesterol, and low-density lipoprotein levels and lower SHBG levels compared with the controls. There was no difference in the serum obesity and inflammatory biomarkers between the PCOS cases and the controls. After adjusting for BMI and age, IL-6 was positively correlated with HOMA, and SHBG was negatively correlated with HOMA, triglyceride, and LDL.
Conclusions: The serum adipokines levels are not good markers for PCOS. PCOS patients were characterized by their high AMH and low SHBG levels. A low level of SHBG should play an important role in the pathogenesis of the medical complications observed in women with PCOS.
Clinical trial registration number NCT01989039.

Introduction

Polycystic ovary syndrome (PCOS) is associated with an adverse cardiometabolic profile consisting of increased total or central adiposity, increased insulin resistance and abnormal glucose metabolism [1]. However, obesity [2] and inflammation [3] might be associated with the pathogenesis of medical complications in women with PCOS.

PCOS induces an increase in serum inflammatory cardiovascular risk markers [4]. Low-grade chronic inflammation in PCOS patients is indicated by the presence of elevated C-reactive protein (CRP) levels and inflammatory cytokines. CRP has been proven to be one of the strongest predictors of the risk of cardiovascular events in patients with or without cardiovascular disease [5]. Furthermore, PCOS is associated with higher anti-Müllerian hormone (AMH) [6] and lower sex hormone-binding globulin (SHBG) [7].

Obesity, characterized by adipocyte hypertrophy, was the major determinant factor for medical and cardiovascular complications among women with PCOS [2]. Adipose tissue can be considered a key endocrine organ because it releases multiple bioactive substances, known as adipose-derived secreted factors or adipokines, with pro-inflammatory or anti-inflammatory activities [8]. Products of adipocytes, such as leptin, adiponectin and resistin, and gut peptides, such as ghrelin, are considered crucial in the interactions between energy balance and reproduction [9]. All of these molecules may lead to local and generalized inflammation,

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http://dx.doi.org/10.1016/j.ejogrb.2015.06.022
0301-2115/

mediating obesity-associated vascular disorders, including hypertension, diabetes, atherosclerosis, and insulin resistance [10]. Dysregulated production or secretion of these adipokines due to adipose tissue dysfunction can contribute to the pathogenesis of obesity-linked complications [8].

Both PCOS and obesity are reported to induce an increase in serum inflammatory cardiovascular risk markers. The precise mechanisms underlying these associations require additional studies to clarify the state of the cardiovascular system in women with PCOS to determine the relative contributions of different factors, including insulin resistance, androgen status and BMI [8]. To understand the insulin resistance and metabolic complications in women of reproductive age, adipokines and inflammatory markers should be treated as important predictors. Therefore, we conducted this study to evaluate the correlation of adipokines and inflammatory markers with insulin resistance in women with PCOS.

Materials and methods

This study was approved by the Institutional Review Board of Taipei Medical University – Wan Fang Hospital, Taipei, Taiwan and was registered at ClinicalTrials.gov with the identifier NCT01989039. We retrospectively reviewed the medical records of female patients who visited our Reproductive Endocrinology Clinic from January 1, 2009, to December 31, 2012.

The study population

Women who had a complete set of anthropometric measurements as well as clinical and biochemical data regarding insulin resistance parameters, inflammatory and obesity biomarkers were initially included in the study. The following data were collected and calculated: (1) obesity hormone levels: adiponectin, leptin, ghrelin, and resistin; (2) inflammatory markers: interleukin (IL)-6 and high-sensitivity C-reactive protein (hs-CRP); (3) anti-müllerian hormone (AMH); (4) serum androgen levels, including total testosterone, androstenedione, dehydroepiandrosterone sulfate (DHEA-S), and the free androgen index (FAI), which was calculated as follows: FAI = total testosterone (nmol/l) × 100/sex hormone binding globulin (SHBG) (nmol/l); (5) insulin sensitivity and glucose tolerance assessments, and (6) lipid profiles, including total cholesterol, triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels. The body mass index (BMI) was defined as the body weight in kilograms divided by the body height in meters squared (kg/m^2). The insulin sensitivity index was evaluated by the homeostasis model assessment insulin resistance index (HOMA) using the following formula:

$$\text{HOMA} = \frac{\text{fasting insulin}\ (\mu\text{U}/\mu\text{L}) \times \text{fasting glucose}\ (\text{mg/dL})}{405}$$

The cut-off value for normal insulin sensitivity in this study was HOMA < 2.14 which based on a previous study of the Chinese population [11].

The following subjects were excluded from the study populations: (1) women who had been diagnosed with malignant tumors, Asherman's syndrome, Mullerian agenesis, or chromosomal anomalies; (2) females younger than 14 or older than 45 years; (3) women who received hormones/drugs for major medical diseases within the previous three months; and (4) women with hyperprolactinemia and premature ovarian failure.

A total of 455 women were initially included for evaluation in the study (Table 1). To make a comparative control group, participants were separated into five subgroups according to their BMI (<20, between 20 and 25, between 25 and 30, between 30 and 35, BMI >35), and women with PCOS and non-PCOS were matched by the values of each BMI subgroup. Ninety cases of PCOS and 35 non-PCOS controls were excluded, and 165 cases of PCOS and 165 non-PCOS controls were finally included (Fig. 1).

Adiponectin, leptin and ghrelin were measured by RIA (LINCO Research, Inc. St. Charles, Missouri, MO, USA), and resistin was measured by enzyme immunoassay (R&D Systems, Inc. Minneapolis, MN, USA).

PCOS was diagnosed according to the Androgen Excess and PCOS Society criteria [12], which requires hyperandrogenism and ovarian dysfunction. Hyperandrogenism (HA) was defined as hirsutism and/or biochemical hyperandrogenaemia (BioHA). The definitions of oligo-anovulation, hyperandrogenism and polycystic ovaries have been described in detail previously [2].

Statistical analysis

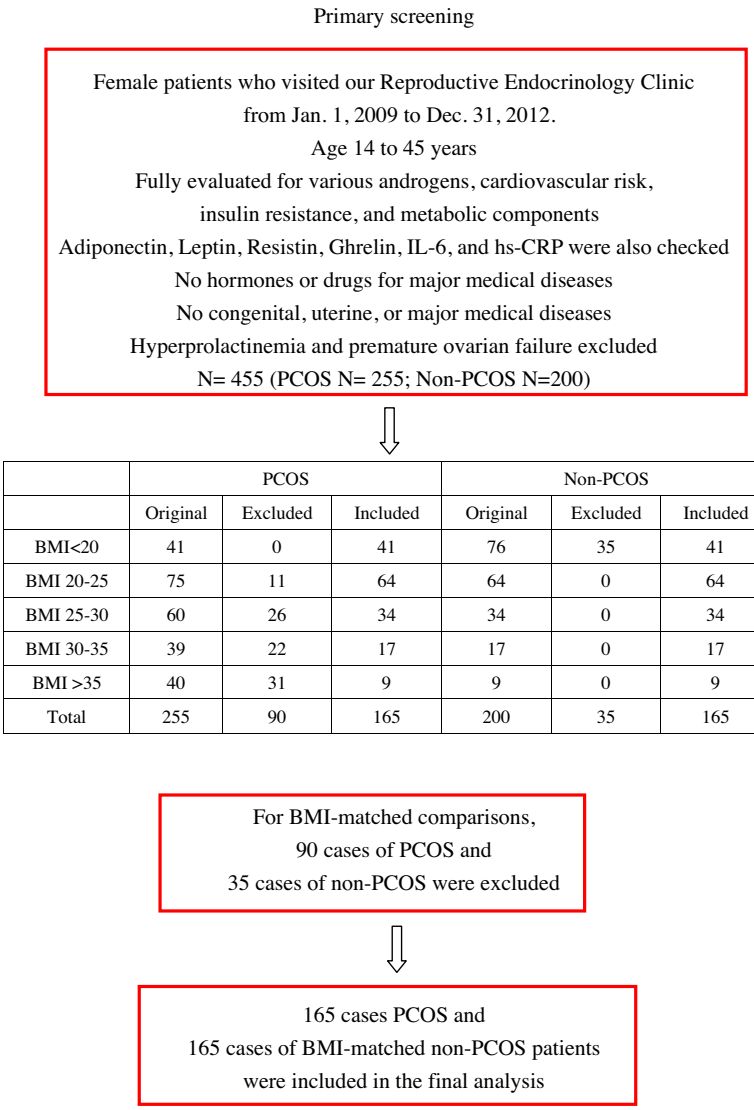
The statistical analysis was performed using SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL, USA). We evaluated the correlation between serum HOMA, total testosterone and inflammatory markers using Pearson's correlation coefficients with the two-tailed method (Table 1). Partial correlations adjusted by age and BMI in the above parameters were also performed. The data are represented as the means ± standard deviation in Tables 1 and 3. We used chi-square and Fisher's exact test to compare categorical variables and ANOVA to compare continuous variables in Tables 1 and 3. Differences

Table 1
Clinical and biomarkers in studied women classified by 5 subgroups of BMI.

	Total	BMI < 25	BMI 20–25	BMI 25–30	BMI 30–35	BMI >35	*p*-value
Case number	455	117	139	94	56	49	<0.001*
PCOS %	56% (255/455)	35% (41/117)	54% (75/139)	64% (60/94)	70% (39/56)	82% (40/49)	<0.001*
Insulin resistance %	52% (236/455)	21% (25/117)	42% (58/139)	65% (61/94)	88% (49/56)	88% (43/49)	
Age (y/o)	27.4 ± 6.5	26.5 ± 6.3	27.3 ± 6.4	27.4 ± 6.5	29.1 ± 6.8	27.6 ± 6.6	0.151
BMI (kg/m^2)	25.3 ± 6.5	18.6 ± 0.9	22.1 ± 1.4	27.3 ± 1.4	32.2 ± 1.2	38.5 ± 3.2	<0.001*
HOMA[a]	3.47 ± 3.71	1.79 ± 2.32	2.08 ± 1.22	4.01 ± 3.80	6.20 ± 3.94	7.27 ± 5.52	<0.001*
SHBG (ng/dL)	42.2 ± 29.6	65.6 ± 33.0	46.7 ± 27.2	30.2 ± 17.2	21.4 ± 8.5	20.5 ± 14.3	<0.001*
hs-CRP (mg/L)	0.25 ± 0.38	0.12 ± 0.38	0.14 ± 0.24	0.24 ± 0.29	0.42 ± 0.34	0.67 ± 0.54	<0.001*
IL-6 (pg/mL)	2.63 ± 4.15	2.35 ± 3.97	2.21 ± 3.26	2.65 ± 3.88	2.47 ± 3.60	4.57 ± 6.77	<0.001*
Adipose tissue components							
Resistin (ng/mL)	10.32 ± 10.46	10.99 ± 9.23	10.41 ± 13.49	10.65 ± 8.18	10.13 ± 10.75	8.06 ± 6.17	0.557
Ghrelin (ng/mL)	598.2 ± 693.3	634.9 ± 568.4	726.6 ± 1091.1	523.1 ± 237.6	455.1 ± 227.7	451.2 ± 241.4	0.029*
Adiponectin (ng/mL)	9181 ± 6090	13,403 ± 6911	9618 ± 6274	7253 ± 3915	5590 ± 2470	5661 ± 2554	<0.001*
Leptin (ng/mL)	15.13 ± 11.99	6.96 ± 4.77	10.41 ± 5.16	18.18 ± 8.60	24.31 ± 11.80	31.70 ± 17.37	<0.001*

Note: Data are either mean ± SD or are percentage; *$p < 0.05$.

[a] Insulin resistance (HOMA > 2.14); The homeostasis model assessment insulin resistance index (HOMA), interleukin (IL)-6, high sensitivity C-reactive protein (hs-CRP), sex hormone-binding globulin (SHBG).



	PCOS			Non-PCOS		
	Original	Excluded	Included	Original	Excluded	Included
BMI<20	41	0	41	76	35	41
BMI 20-25	75	11	64	64	0	64
BMI 25-30	60	26	34	34	0	34
BMI 30-35	39	22	17	17	0	17
BMI >35	40	31	9	9	0	9
Total	255	90	165	200	35	165

Fig. 1. Flow chart of patient selection used in this study.

between groups were considered significant if the corresponding p-values were <0.05.

Results

The prevalence of PCOS and insulin resistance were highly BMI dependant. Table 1 showed 455 women contained 56% (255/455) of PCOS and 52% (255/455) of insulin resistance in Table 1, the prevalence of PCOS for women with BMI <25, BMI between 20 and 25, BMI between 25 and 30, BMI between 30 and 35, and BMI >35 were 35% (41/117), 54% (75/139), 64% (60/94), 70% (39/56) and 82% (40/49) respectively. Similarly, the prevalence of insulin resistance for women with BMI <25, BMI between 20 and 25, BMI between 25 and 30, BMI between 30 and 35, and BMI >35 were 21% (25/117), 42% (58/139), 65% (61/94), 88% (49/56), and 88% (43/49) respectively.

Fig. 1 demonstrates the selection of BMI matched studied groups between women with and without PCOS, 165 cases of PCOS and 165 non-PCOS controls were finally included.

Table 2 presents the correlation between insulin resistance (HOMA), total testosterone levels, and BMI with various obesity biomarkers. The results demonstrated that adiponectin was negatively correlated with HOMA, BMI, and the total testosterone, triglyceride, and leptin levels (all $p < 0.001$); conversely, the leptin levels were significantly positively correlated with HOMA, BMI, and the total testosterone and triglyceride levels (all $p < 0.001$).

Partial correlation analysis was applied after adjusting for BMI and age. The IL-6 levels were positively correlated with HOMA ($\mu = 0.120$, $p = 0.030$). The SHBG levels were negatively correlated with the levels of HOMA ($\mu = -0.128$, $p = 0.020$), triglyceride ($\mu = -0.241$, $p < 0.001$), and LDL ($\mu = -0.178$, $p = 0.001$). The adiponectin levels were negatively correlated with the triglyceride levels ($\mu = -0.223$, $p < 0.001$) and positively correlated with the HDL levels ($\mu = 0.363$, $p < 0.001$). The resistin levels were positively correlated with the adiponectin levels ($\mu = 0.155$, $p = 0.005$) and negatively correlated with the testosterone levels ($\mu = -0.136$, $p = 0.014$).

Table 3 shows the results of various parameters in women with PCOS vs. non-PCOS controls. Women with PCOS had significantly higher levels of fasting insulin, total cholesterols, and LDL compared to the controls. Women with PCOS had significantly lower levels of SHBG and higher levels of AMH than the controls; however, the serum adiponectin, leptin, resistin, ghrelin, hs-CRP and IL-6 levels were not different between the two groups.

Table 2
Pearson correlation between insulin resistance, total testosterone, and body mass index with various obesity and inflammatory biomarkers.

		HOMA[a]	BMI[a]	Age	Testosterone	Resistin	Ghrelin	Adiponectin	Leptin	hs-CRP[a]	IL-6[a]	Triglyceride	AMH[a]	SHBG[a]
HOMA[a]	1													
BMI[a]	γ	0.481*	1											
	p-value	<0.001												
Age	γ	−0.004	0.233*	1										
	p-value	0.945	<0.001											
Testosterone	γ	0.154*	0.209*	−0.104	1									
	p-value	0.005	<0.001	0.059										
Resistin	γ	0.077	0.003	−0.025	−0.126*	1								
	p-value	0.164	0.954	0.653	0.022									
Ghrelin	γ	−0.046	−0.105	−0.001	−0.066	0.005	1							
	p-value	0.406	0.056	0.982	0.229	0.925								
Adiponectin	γ	−0.251*	−0.405*	−0.256*	−0.143*	0.142*	0.026	1						
	p-value	<0.001	<0.001	<0.001	0.009	0.010	0.642							
Leptin	γ	0.374*	0.685*	0.137*	0.283*	0.046	−0.130*	−0.239*	1					
	p-value	<0.001	<0.001	0.013	<0.001	0.403	0.018	<0.001						
hs-CRP[a]	γ	0.192*	0.405*	0.147*	0.013	0.084	−0.085	−0.088	0.281*	1				
	p-value	<0.001	<0.001	0.008	0.818	0.127	0.123	0.112	<0.001					
IL-6[a]	γ	0.140*	0.063	−0.035	−0.021	−0.001	0.020	−0.005	0.106	0.090	1			
	p-value	0.011	0.252	0.521	0.709	0.986	0.717	0.932	0.054	0.102				
Triglycerides	γ	−0.341*	0.361*	0.207*	0.177*	−0.012	−0.076	−0.352*	0.208*	0.160*	0.010	1		
	p-value	<0.001	<0.001	<0.001	0.001	0.826	0.168	<0.001	<0.001*	0.004	0.851			
AMH[a]	γ	−0.067	−0.176*	−0.179*	0.479*	−0.015	0.014	0.090	−0.063	−0.102	0.061	−0.008	1	
	p-value	0.223	0.001	0.001	<0.001	0.793	0.807	0.101	0.257	0.063	0.272	0.882		
SHBG[a]	γ	−0.330*	−0.449*	0.028	−0.212*	0.073	0.044	0.317*	−0.317*	0.201*	−0.002	−0.342*	0.009	1
	p-value	<0.001	<0.001	0.617	<0.001	0.188	0.421	<0.001	<0.001	<0.001	0.972	<0.001	0.330	

* $p < 0.05$.
[a] The homeostasis model assessment insulin resistance index (HOMA), body mass index (BMI), interleukin (IL)-6, high sensitivity C-reactive protein (hs-CRP); anti-müllerian hormone (AMH), sex hormone binding globulin (SHBG)

Comments

Both obesity and inflammation contribute to the metabolic complications for women of reproductive age. The state of the cardiovascular system in women with PCOS might be due to different factors, including insulin resistance, androgen status and BMI [4]. Excess androgen should be the most important component of PCOS [13]. AMH is the indicator of ovarian reservation and polycystic ovary morphology [6]. This study attempted to evaluate the obesity and inflammatory biomarkers predictive of PCOS and insulin resistance. In previous studies [2], we found that BMI is the predominant factor for medical complications in women of

Table 3
A comparison of various biomarkers in women with and without PCOS.

	Total	PCOS	Non-PCOS	p-value
Case number	330	165	165	
Age (y/o)	27.8 ± 6.4	27.0 ± 5.7	28.6 ± 6.9	0.023*
Menarche (y/o)	12.6 ± 1.5	12.7 ± 1.5	12.6 ± 1.5	0.550
BMI (kg/m^2)	24.3 ± 5.7	24.4 ± 5.8	24.1 ± 5.6	0.674
Anti-Müllerian hormone (ng/mL)	7.7 ± 5.4	9.7 ± 5.7	5.8 ± 4.3	<0.001*
SHBG (ng/dL)	43.3 ± 27.4	37.6 ± 23.4	49.1 ± 29.8	<0.001*
hs-CRP (mg/L)	0.21 ± 0.36	0.21 ± 0.33	0.21 ± 0.38	0.977
IL-6 (pg/mL)	2.5 ± 3.6	2.7 ± 4.2	2.4 ± 2.9	0.455
Adipose tissue components				
Resistin (ng/mL)	10.4 ± 9.3	9.6 ± 9.4	11.3 ± 9.1	0.089
Ghrelin (ng/mL)	595.6 ± 727.1	587.8 ± 809.3	603.3 ± 636.8	0.847
Adiponectin (ng/mL)	9414 ± 6222	9213 ± 6843	9615 ± 5546	0.558
Leptin (ng/mL)	13.6 ± 10.4	14.4 ± 10.9	12.7 ± 9.8	0.138
Androgens				
Total testosterone (nmol/L)	2.11 ± 1.02	2.56 ± 1.04	1.67 ± 0.77	<0.001*
Androstenedione (nmol/L)	9.39 ± 4.70	10.90 ± 4.85	7.88 ± 4.02	<0.001*
Free androgen index	7.64 ± 7.35	10.05 ± 7.93	5.22 ± 5.81	<0.001*
DHEAS (nmol/L)	5294 ± 2751	5509 ± 2539	5080 ± 2940	0.157
Insulin sensitivity and glucose tolerance				
Fasting insulin (pmol/L)	92.4 ± 97.1	103.7 ± 119.0	81.0 ± 67.2	0.034*
Fasting glucose (mmol/L)	5.12 ± 1.04	5.09 ± 0.72	5.15 ± 1.29	0.605
2-Hour glucose (mmol/L)	6.27 ± 2.74	6.17 ± 2.34	6.37 ± 3.09	0.507
HOMA[a]	3.15 ± 3.48	3.48 ± 4.04	2.81 ± 2.78	0.079
Lipid profiles and blood pressure				
Cholesterol (mmol/L)	4.84 ± 0.91	5.00 ± 0.90	4.69 ± 0.89	0.002*
Triglycerides (mmol/L)	1.05 ± 0.87	1.20 ± 1.06	0.91 ± 0.58	0.002*
HDL (mmol/L)	1.40 ± 0.40	1.40 ± 0.39	1.40 ± 0.41	0.984
LDL (mmol/L)	2.88 ± 0.81	2.99 ± 0.83	2.77 ± 0.78	0.013*

Note: Data are either mean ± SD or are percentage; *$p < 0.05$.
[a] The homeostasis model assessment insulin resistance index (HOMA), dehydroepiandrosterone sulfate (DHEA-S), the free androgen index (FAI), high-density lipoprotein (HDL), low-density lipoprotein (LDL), interleukin (IL)-6, high sensitivity C-reactive protein (hs-CRP), sex hormone-binding globulin (SHBG).

reproductive age; therefore, this study compared BMI-matched cases and controls.

The association between inflammatory processes and PCOS is a controversial issue [14]. Escobar-Morreale suggested that women with PCOS exhibit an elevation in circulating CRP that is independent of obesity [3]. On the contrary, Puder suggested that increases in low-grade chronic inflammation and insulin resistance in women with PCOS are primarily associated with increased central excess fat rather than PCOS status [15]. Our study suggested various inflammatory markers that might play different roles and should be considerate separately. Elevated hs-CRP was associated with cardiovascular risk factors [5]. IL-6 is a key pro-inflammatory and immune-modulatory cytokine of relevance for cardiovascular (CD) diseases [16]. Although hs-CRP and IL-6 were both correlated with insulin resistance, our results showed that the association between hs-CRP and insulin resistance were BMI-dependent, but the association between insulin resistance with IL-6 was BMI-independent. Fulghesu suggest that IL-6 is correlated with insulin resistance in PCOS patients and that an altered immune response to inflammatory stimuli is present in the insulin resistance of PCOS patients [17]. Tarkun demonstrated that IL-6 concentrations are elevated in normal weight women with PCOS, which may contribute to the evidence of insulin resistance in lean women with PCOS [18]. The pathogenesis for IL-6 and insulin resistance in women with PCOS needs to be further explored.

Adiponectin and leptin are both adipocyte-derived hormones that are highly correlated with the BMI. Several studies from different laboratories have highlighted the potential antidiabetic, antiatherosclerotic and anti-inflammatory properties of adiponectin [19]. Leptin, an adipocyte-derived hormone, serves as a link relaying metabolic signals to the neuronal networks in the brain [20]. The adiponectin- and leptin-mediated reversal of insulin resistance and lipid profiles was also confirmed in our study. The adiponectin concentrations were inversely correlated with the BMI, HOMA, and the testosterone and triglyceride levels. On the contrary, the leptin concentrations were correlated positively with the above-mentioned parameters. However, the serum adiponectin and leptin levels were not different between women with and without PCOS.

Unlike adiponectin and leptin, the serum resistin and ghrelin levels were not associated with BMI in our study. Resistin is an adipocyte- and monocyte-derived cytokine that has been implicated in the modulation of insulin action, energy, glucose and lipid homeostasis [21]. Although resistin expression was initially defined in adipocytes, the major cell populations that express and produce resistin in humans are mononuclear leukocytes, macrophages, and splenic and bone marrow cells [22]. Resistin has been initially postulated to be a risk factor for insulin resistance; however, the subsequent available data on this cytokine have revealed contradictory findings in both humans and rodents [23]. We could not demonstrate a correlation between the serum resistin levels and insulin resistance. Furthermore, our results showed that the serum resistin levels are positively correlated with adiponectin and negatively correlated with the total testosterone levels; this relationship persisted even after adjusting for BMI and age. The complicated and controversial relationship of the serum resistin levels with medical complications should be explored in future studies.

Ghrelin is a natural ligand of the growth hormone secretagogue receptor and is a potent stimulant of GH secretion. Ghrelin plays a role in regulating glucose metabolism and energy balance. Although the results demonstrated that the serum ghrelin levels are negatively correlated with the leptin levels, our study could not determine any differences in the serum ghrelin levels between women with PCOS and the controls. Similarly, Skommer found that polycystic ovaries exhibit expression levels of ghrelin mRNA that are nearly ten times lower than those found in normal ovaries, whereas the mRNA levels in blood cells were similar in both study groups; therefore, he suggested that the presence of ghrelin in PCOS patients may have an autocrine/paracrine modulatory effect on ovary function and a local significance in the etiology of PCOS [24].

Sex hormones may influence risk factors for noninsulin-dependent diabetes mellitus (NIDDM). The serum SHBG levels were negatively correlated with insulin resistance, BMI, and the testosterone, leptin and triglyceride levels. After adjusting for age and BMI, SHBG was still negatively correlated with insulin resistance and the triglyceride and LDL levels. Our results showed that women with PCOS presented with lower serum SHBG than the controls. Low SHBG levels result in a larger fraction of unbound testosterone, further increasing the biological androgen excess in women with PCOS. Therefore, we hypothesize that low SHBG levels play an important role in the pathogenesis of insulin resistance and cardiovascular disease in women with PCOS.

Adipocytokines and inflammatory cytokines act in an autocrine, paracrine, and endocrine manner [10]. The serum adipose and inflammatory biomarker levels might not reflect the true roles of their reactions in tissue levels. However, the serum levels of biomarkers still provide important information for understanding the pathological condition of disease. This study evaluated multiple biomarkers using a large sample size with BMI-matched controls. Our results also showed correlations between various biomarkers with metabolic parameters. Although the actual mechanism of each biomarker could not be understood in full, the different characteristics of various biomarkers were addressed. The medical complications contributing to PCOS or obesity were very similar and often confused. To eliminate cross reaction with obesity, some BMI-independent biomarkers might be useful in attempting to understand the risks of medical complications that contribute to the pathogenesis of PCOS.

The major weakness of this study is that the women evaluated were recruited from the outpatient clinic of the University Hospital and do not reflect the true distribution of the general population. Therefore, these results should be applied to the general population with caution. However, to the best of our knowledge, this is the study with the largest sample size with BMI-matched controls to evaluate multiple inflammatory and adipose biomarkers in women with PCOS.

Conclusions

1. Women with PCOS presented with higher total cholesterol, triglyceride, and LDL levels than women without PCOS.
2. PCOS patients were characterized by high levels of AMH and low levels of SHBG; however, the serum adiponectin, leptin, resistin, ghrelin, IL-6, and hs-CRP levels were not significantly different between women with PCOS and the controls.
3. The serum hs-CRP, adiponectin and leptin levels were highly BMI-dependent, but IL-6, resistin and ghrelin were not.
4. The reversal reactions between adiponectin and leptin were very clear, but the impact of resistin on women's health remains a controversy.
5. Although hs-CRP and IL-6 were both correlated with insulin resistance, the association between hs-CRP and insulin resistance was BMI-dependent, but the association between insulin resistance with IL-6 was BMI-independent.
6. Low SHBG, independent of BMI, was associated with lipid dysfunction. Low SHBG should play an important role in the pathogenesis of medical complications from PCOS.

Acknowledgements

This work was supported by the Taiwan National Science Council Grant NSC 102-2629-B-038-001 and Taipei Medical University – Wan Fang Hospital Grant 103-wf-eva-10.

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