Research Article

Body Composition Parameters, Adiponectin, Leptin and Adiponectin/ Leptin Ratio are Correlated with LH/FSH Ratio in Women with PCOS but not in Women without PCOS

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Abstract

Objective: To investigate the correlation between body composition parameters, adiponectin, leptin and the adiponectin/ leptin ratio and the LH/FSH ratio in women with polycystic ovary syndrome (PCOS).

Methods: A cross-sectional study was conducted at Reproductive Cluster Yasmin, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, with sixty women with PCOS and sixty healthy women as controls (matched for age and BMI). Body composition parameters, including body weight, body mass index (BMI), waist circumference (WC), waist to hip ratio (WHR), percent body fat (PBF), visceral fat area (VFA), percent subcutaneous fat (PSF) and skeletal muscle mass (SMM), were measured; levels of fasting glucose, fasting insulin, testosterone, and sex hormone binding globulin (SHBG) were measured; and homeostatic model assessment for insulin resistance (HOMA-IR) values, anti-Mullerian hormone (AMH), free androgen index (FAI), Ferriman-Gallwey (FG) score, adiponectin levels, leptin levels, adiponectin/leptin ratio, LH, FSH and LH/FSH ratio were measured.

Results: Body composition parameters (body weight, BMI, WC, WHR, PBF, VFA, PSF, SMM) were not significantly different between women with PCOS and controls. Fasting insulin ($P<0.05$), HOMA-IR ($P<0.05$), AMH ($P<0.01$), FAI ($P<0.01$), FG score ($P<0.01$) and LH/FSH ratio ($P<0.05$) were higher in PCOS women. Adiponectin ($P<0.01$) was lower in PCOS women, while leptin and the adiponectin/leptin ratio were not significantly different between groups. Most of body composition parameters, adiponectin, leptin and adiponectin/leptin ratio were correlated with HOMA-IR in both groups. SMM was positively correlated with the LH/FSH ratio, while body weight, BMI, WC, PBF, VFA, and PSF were inversely correlated with the LH/FSH ratio in PCOS patients but not in controls. WHR was not correlated in either group. Leptin ($r=-0.278$; $P<0.05$) was negatively correlated with the LH/FSH ratio only in the PCOS group. Adiponectin ($r=0.394$; $P<0.01$) and the adiponectin/leptin ratio ($r=0.413$; $P<0.01$) were also positively correlated with the LH/FSH ratio only in the PCOS group. AMH was correlated with the LH/FSH ratio, whereas testosterone level, FAI, FG score, fasting insulin level and HOMA-IR value were not correlated with the LH/FSH ratio in PCOS women.

Conclusion: Most of the body composition parameters, leptin, adiponectin and the adiponectin/leptin ratio were significantly correlated with HOMA-IR in both groups. However, correlations of those parameters with LH/FSH ratio were found only in PCOS but not in women without PCOS. Adiponectin and leptin may play a significant role in the mechanism of neuroendocrine disorders in PCOS, which is characterized by an increased LH/FSH ratio.

Keywords: adiponectin, adiponectin/leptin ratio, body composition, HOMA-IR, leptin, LH/FSH ratio, PCOS.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is known to be the most common endocrine disorder in women of reproductive age, with a prevalence of approximately 5 to 20%.[1] The clinical features of PCOS include menstrual irregularity, hirsutism and infertility.[2] Obesity and insulin resistance are metabolic disorders that are often found in women with PCOS.[3] In addition, the presence of neuroendocrinological disorders in the form of increased LH levels and the LH/FSH ratio is commonly encountered in women with PCOS.[4] Both insulin resistance and an increased LH/FSH ratio are associated with chronic anovulation, hyperandrogenemia, polycystic morphology of the ovary, increased levels of AMH and disruption of the sex hormone feedback mechanism to the pituitary and hypothalamus.[5,6] Therefore, insulin resistance and an increased LH/FSH ratio, among other factors such as genetic, epigenetic and environmental factors, are thought to be important parts of the complex pathogenesis of PCOS.

Previous studies have shown a strong relationship between dysregulated adipokine expression and the onset of glucose intolerance and insulin resistance in PCOS women.[7,8] Adipose tissue secretes adipokines, most notably leptin and adiponectin.[9,10] Leptin is thought to be importantly involved in regulating food intake, metabolism, and reproduction. Some studies found significantly higher leptin levels in PCOS women than in those who have regular menstruation, and leptin levels were positively correlated with insulin resistance.[9-11] A study shows that giving insulin sensitizer can reduce leptin and insulin levels and improve reproductive function in PCOS patients.[12] In contrast, adiponectin improves insulin sensitivity and has an anti-inflammatory effect. Previous studies have shown a reduction in adiponectin levels in PCOS women with insulin resistance and obesity.[10,13-15] Furthermore, the adiponectin/leptin ratio is considered a potent indicator of insulin resistance and has the potential to be used as a marker of PCOS.[10] The association between adipokines and neuroendocrine disorders in PCOS has also been studied previously.[11,16,17]

Studies have demonstrated that visceral obesity is associated with an elevated risk of metabolic syndrome.[18-20] Measurement of body weight or BMI alone cannot describe the distribution of fat mass from different body parts and cannot predict the occurrence of insulin resistance. Therefore, body composition measurements are considered a better method to differentiate peripheral and visceral body fat, as well as fat-free mass, and to predict the risk of metabolic disorders in PCOS women.[21] Body composition can be easily measured using bioelectrical impedance analysis, which is noninvasive, inexpensive and reliable.[22] Studies have demonstrated that body composition parameters are different between women with PCOS and controls. Moreover, body composition parameters were correlated with increased leptin levels and lower adiponectin levels in PCOS women.[23-25]

Obesity and metabolic syndrome, particularly insulin resistance, have become epidemic diseases and are closely linked to the prevalence of PCOS. Given the ongoing development of the theory on PCOS pathogenesis, it is crucial to conduct further research exploring the relationship between anthropometric profiles and adipokines in connection with insulin resistance and the LH/FSH ratio. Therefore, this current study aimed to investigate the correlation between body mass composition parameters, levels of leptin and adiponectin, the adiponectin/leptin ratio, and HOMA-IR values, as well as the LH/FSH ratio in women with PCOS.

METHODS

Sample Collection

PCOS was diagnosed according to the Revised 2003 consensus on diagnostic criteria (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group 2004)[2], identified as any two of the following three criteria: clinical and/or biochemical signs of hyperandrogenism, oligo- or anovulation, and polycystic ovarian morphology determined by ultrasonography. This is a cross-sectional study with a total of 120 women of reproductive age divided into two groups of sixty, one with PCOS and the other as controls. Based on the sample size formula for this study, the minimum sample needed reached 56 samples with SD from previous research of 14.96 and the proportion difference from this study of 10.01; hence, the study settled with sixty samples. The samples were recruited from the Yasmin Clinic, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, from September

2021 until August 2022. Patients with any other cause of hyperandrogenism or oligomenorrhea, such as Cushing's syndrome, congenital adrenal hyperplasia, hypothyroidism, or significant increases in serum prolactin levels, were excluded. In addition to the exclusion criteria, no subjects had taken medications known to disrupt the function of the HPG axis, such as corticosteroid, hormonal therapy, antiepileptic, or antipsychotic drugs in the last 6 months.

The subjects were taken using consecutive sampling technique until the minimum number of samples have been reached. The enrolled patients underwent comprehensive physical examination, USG, and laboratory examination. Another sixty healthy women without both menstrual disturbance and hyperandrogenism were recruited as controls. Both groups of PCOS and controls were then divided equally into two groups based on their body mass index (BMI) according to the Asia Pacific criteria, which states that normal weight is classified as 18.5-22.9 kg/ m^2 and obese is classified as more than 25 kg/ m^2. From all subjects, 5 ml whole-blood samples were obtained in the follicular phase (until Day 5 of the menstrual cycle) after overnight fasting (10 to 12 h). Fasting was done to have accurate results for fasting glucose and fasting insulin levels to evaluate HOMA-IR. The Ferriman-Gallwey (FG) score and free androgen index (FAI) were calculated to investigate hyperandrogenism. The FG score was evaluated by measuring terminal hair growth on eleven different body areas with a scale from 0 to 4 each based on the FG scoring system and the cut off found for PCOS in Asia.[26] FAI is a measurement of the biologically active testosterone levels in the blood, evaluated by multiplying 100 with the total testosterone level divided with the SHBG level. Homeostatic model assessment for insulin resistance (HOMA-IR) was measured to investigate insulin resistance. This study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital (KET-/197/ UN2.F1/ETIK/PPM.00.02/2021). Written informed consent was obtained from each subject.

Hormone, Glucose, and SHBG Measurements

The levels of total testosterone (T), luteinizing hormone (LH), follicle-stimulating hormone (FSH), fasting insulin, anti-Müllerian hormone (AMH), and sex-hormone binding globulin (SHBG) were measured using TOSOH (Tosoh India Pvt. Ltd., Mumbai, India) following the manufacturer's protocols. All samples intended for examination were previously thawed, diluted, and then placed into a 500 µl sample cap. Subsequently, the sample cap and reagent were inserted into the instrument. The diluent was filled, the buffer tank was washed, and the waste tank was emptied. The sample identity was entered into the software, followed by pressing the start button on the instrument, leading to the appearance of the hormone level results. Additionally, the levels of adiponectin, leptin, and fasting glucose were measured using ELISA kits based on each component utilizing the sandwich ELISA principle.

Assessment of Body Composition

Body composition parameters were measured using the bioimpedance method with an Omron HBF 375 (Omron Body Fat Analyzer HBF-375; Omron, Bannockburn, Illinois) according to the instructions provided by the manufacturer. The selected body composition parameters measured in this study were weight (kg), BMI (kg/m^2), percent body fat (PBF) (%), visceral fat area (VFA) (cm^2), percent subcutaneous fat (PSF) (%), and skeletal muscle mass (SMM) (kg). Waist circumference (WC) was measured between the iliac crest's superior border and the ribs' inferior border using a tape measure with subjects standing, whereas hip circumference (HC) was measured over the buttocks at the maximum circumference. The waist-to-hip ratio (WHR) is defined as WC/HC.

Statistical Analysis

The data are presented as the mean ± SE (standard error) for demographic and endocrine characteristics. The collected data were normalized using the Kolmogorov–Smirnov test to determine the data distribution. Correlation tests between the dependent and independent variables were performed using the Pearson test if both numeric variables tested had a normal distribution or using the Spearman test if they did not have a normal distribution. A value of $p < 0.05$ was considered to indicate significance. The statistical analysis was performed using SPSS version 26.0.

RESULTS

The demographic and endocrine characteristics of women with PCOS and the control women are presented in Table 1. Compared to controls, body composition parameters (weight, BMI, WC, WHR, PBF, VFA, PSF, SMM) did not significantly differ between women with PCOS and controls (Table 1). Fasting glucose was not significantly different, but fasting insulin levels (P<0.05) and HOMA-IR value (P<0.05) were elevated in PCOS women; therefore, insulin resistance was significantly increased in PCOS women compared to controls. AMH was significantly elevated in PCOS women compared with controls (P<0.01). Testosterone and SHBG did not significantly differ between the two groups; however, the FAI (P<0.01) and FG score (P<0.01) were significantly higher in women with PCOS. Adiponectin (P<0.01) levels were significantly decreased in PCOS women, while leptin levels and the adiponectin/leptin ratio were not significantly different between groups. LH and FSH were not significantly different between groups, while the LH/FSH ratio was significantly higher in the PCOS group.

Table 1. Characteristics of Women with and without PCOS

Characteristics	PCOS (Mean ± SE)	Non PCOS (Mean ± SE)	*P-value*
Age (years)	26.02 ± 0.45	25.47 ± 0.57	0.452
Weight (kg)	64.47 ± 1.83	74.48 ± 12.30	0.422
BMI (kg/m^2)	26.19 ± 0.75	24.42 ± 0.80	0.109
WC (cm)	81.70 ± 1.65	79.07 ± 1.50	0.242
WHR	0.81 ± 0.08	0.81 ± 0.08	0.611
PBF (%)	32.69 ± 0.76	32.58 ± 0.73	0.916
VFA (cm^2)	7.37 ± 0.76	6.14 ± 0.62	0.212
PSF (%)	29.82 ± 0.85	28.97 ± 0.80	0.465
SMM (kg)	24.37 ± 0.31	25.15 ± 0.41	0.128
Fasting glucose (mg/dL)	95.61 ± 1.29	93.08 ± 1.11	0.140
Fasting insulin (uIU/mL)	15.11 ± 2.41	9.32 ± 0.88	0.026*
HOMA-IR (%)	3.49 ± 0.58	2.19 ± 1.62	0.036*
AMH (ng/mL)	12.66 ± 0.92	4.99 ± 0.38	0.000**
Testosterone (ng/dL)	76.68 ± 5.44	57.09 ± 9.32	0.072
SHBG (nmol/L)	51.92 ± 8.42	71.32 ± 5.10	0.051
FAI	7.92 ± 0.82	4.03 ± 0.66	0.000**
FG score	6.47 ± 0.37	3.19 ± 0.31	0.000**
Adiponectin (ng/mL)	4.88 ± 0.33	6.95 ± 0.49	0.001**
Leptin (ng/mL)	6.99 ± 0.60	5.65 ± 0.54	0.101
Adiponectin/Leptin ratio	1.51 ± 0.31	5.63 ± 2.98	0.172
LH (mIU/mL)	10.56 ± 0.65	9.94 ± 3.17	0.850
FSH (mIU/mL)	7.09 ± 0.26	6.69 ± 0.54	0.514
LH/FSH ratio	1.49 ± 0.07	1.11 ± 0.16	0.033**

Note: BMI=body mass index; WC=waist circumference; WHR=waist:hip ratio; PBF=percent body fat; VFA=visceral fat area; PSF=percent subcutaneous fat; SMM=skeletal muscle mass; HOMA-IR= homeostatic model assessment for insulin resistance; LH=luteinizing hormone; FSH=follicle stimulating hormone; SHBG=sex hormone binding globulin; FAI=free androgen index; FG score=Ferriman Gallwey score.*P<0.05 = significant difference. **P<0.01 = significant difference.

A subgroup analysis was performed based on BMI (lean and obese PCOS), as shown in Table 2. WC (P<0.01), PBF (P<0.01), VFA (P<0.01) and PSF (P<0.01) were higher in the obese group, while SMM (P<0.01) was higher in the lean PCOS group. Interestingly, the WHR was similar between the 2 groups. Fasting insulin levels (P<0.01) and HOMA-IR value (P<0.01) were elevated in obese PCOS patients, while fasting glucose levels were not different between the groups. FAI (P<0.01) was elevated in obese women, SHBG (P<0.01) was higher in lean PCOS women, and AMH and testosterone levels were not significantly different between groups. Significant differences in adiponectin, leptin, and the adiponectin/leptin ratio (P<0.01) between the two groups were also observed. Adiponectin levels (P<0.01) and the adiponectin/leptin ratio (P<0.01) were lower in obese subjects, whereas leptin levels (P<0.01) were higher. Interestingly, the LH/FSH ratio (P<0.05) was elevated in lean compared to obese PCOS patients.

Table 2. Characteristics of Obese and Lean PCOS Women

Characteristics	PCOS group (Mean ± SE)		*P-value*
	Obese (n = 30)	Lean (n = 30)	
Age (years)	26.23 ± 0.65	26.03 ± 0.52	0.638
Weight (kg)	76.07 ± 1.87	52.86 ± 0.94	0.000**
BMI (kg/m2)	30.94 ± 0.79	20.53 ± 0.28	0.000**
WC (cm)	91.67 ± 1.78	71.73 ± 1.02	0.000**
WHR	0.83 ± 0.01	0.81 ± 0.10	0.083
PBF (%)	37.3 ± 0.71	28.10 ± 0.60	0.000**
VFA (cm2)	11.77 ± 0.99	2.99 ± 0.21	0.000**
PSF (%)	35.03 ± 0.86	24.61 ± 2.95	0.000**
SMM (kg)	22.85 ± 0.38	25.89 ± 1.57	0.000**
Fasting glucose (mg/dL)	94.10 ± 1.29	91.03 ± 1.41	0.223
Fasting insulin (uIU/mL)	22.60 ± 4.36	6.80 ± 0.67	0.001**
HOMA-IR (%)	5.16 ± 1.05	1.81 ± 0.21	0.003**
AMH (ng/mL)	12.00 ± 1.28	13.31 ± 1.33	0.479
Testosterone (ng/dL)	73.52 ± 7.45	62.75 ± 5.34	0.566
SHBG (nmol/L)	27.99 ± 1.83	78.60 ± 7.85	0.004**
FAI	10.30 ± 1.30	5.75 ± 1.18	0.003**
FG score	6.6 ± 0.56	6.33 ± 0.48	0.721
Adiponectin (µg/mL)	3.85 ± 0.35	5.90 ± 0.49	0.001**
Leptin (ng/mL)	9.78 ± 0.86	4.21 ± 0.45	0.000**
Adiponectin/Leptin ratio	0.51 ± 0.08	2.51 ± 0.56	0.001**
LH (mIU/mL)	9.58 ± 0.87	11.54 ± 0.94	0.129
FSH (mIU/mL)	7.16 ± 0.32	6.45 ± 0.51	0.788
LH/FSH ratio	1.32 ± 0.08	1.90 ± 0.12	0.017*

Note: BMI=body mass index; WC=waist circumference; WHR=waist:hip ratio; PBF=percent body fat; VFA=visceral fat area; PSF=percent subcutaneous fat; SMM=skeletal muscle mass; HOMA-IR= homeostatic model assessment for insulin resistance; LH=luteinizing hormone; FSH=follicle stimulating hormone; SHBG=sex hormone binding globulin; FAI=free androgen index; FG score=Ferriman Gallwey score. *P<0.05 = significant difference. **P<0.01 = significant difference.

Body weight, BMI, WC, PBF, VFA and PSF had a significant positive correlation, while SMM had a negative correlation with HOMA-IR value in both PCOS women and controls, as shown in Table 3. However, WHR only had a significant positive correlation with HOMA-IR value in PCOS women. Testosterone had a negative correlation with HOMA-IR value only in the PCOS group, while FAI was positively correlated with HOMA-IR value only in the control group. SHBG had a negative correlation with HOMA-IR value in both groups, while AMH and FG scores did not correlate with HOMA-IR value in either group. Fasting insulin had a positive correlation with HOMA-IR value in both groups, whereas fasting glucose was not correlated with HOMA-IR value in either group. Leptin levels in women with PCOS and controls had a positive correlation with HOMA-IR, while adiponectin levels were negatively correlated with HOMA-IR value in both groups.

Body weight, BMI, WC, PBF, VFA, and PSF were negatively correlated with the LH/FSH ratio, while SMM was positively correlated with the LH/FSH ratio only in PCOS patients, while WHR was not correlated with the LH/FSH ratio in either group. FG score, testosterone, SHBG and FAI scores did not correlate with the LH/FSH ratio in PCOS patients and controls. Fasting glucose was positively correlated with the LH/FSH ratio only in PCOS patients; in contrast, fasting insulin was correlated with the LH/FSH ratio only in the control group. HOMA-IR value did not correlate with the LH/FSH ratio in either group. AMH also had a positive correlation with the LH/FSH ratio in PCOS women but not in controls. This study also found that leptin levels had a negative correlation with the LH/FSH ratio only in the PCOS group. Interestingly, adiponectin levels and the adiponectin/leptin ratio were also found to only positively correlate with the LH/FSH ratio in the PCOS group, not in the control group.

Table 3. Correlation between Metabolic Characteristics and LH/FSH Ratio and HOMA-IR Value in Women with and without PCOS

Characteristics	HOMA-IR				LH/FSH Ratio			
	PCOS (n = 60)		Control(n = 60)		PCOS (n = 60)		Control(n = 60)	
	r	p-value	r	p-value	r	p-value	r	p-value
Age (years)	0.020	0.878	-0.127	0.334	0.151	0.251	-0.025	0.847
Weight (kg)	0.618	0.000**	0.478	0.000**	-0.365	0.004**	-0.028	0.831
BMI (kg/m^2)	0.626	0.000**	0.361	0.005**	-0.373	0.003**	-0.044	0.739
WC (cm)	0.637	0.000**	0.441	0.000**	-0.324	0.011*	-0.111	0.399
WHR	0.268	0.038*	0.120	0.359	-0.017	0.895	-0.071	0.591
PBF (%)	0.604	0.000**	0.347	0.007**	-0.333	0.009**	-0.001	0.997
VFA (cm2)	0.561	0.000**	0.449	0.000**	-0.349	0.006**	-0.055	0.674
PSF (%)	0.668	0.000**	0.491	0.000**	-0.335	0.009**	-0.046	0.725
SMM (%)	-0.572	0.000**	-0.324	0.012*	0.294	0.023*	-0.036	0.786
FG score	-0.110	0.402	0.294	0.056	0.071	0.591	-0.046	0.769
Testosterone (ng/dL)	-0.419	0.001**	0.121	0.359	0.242	0.062	0.234	0.071
SHBG (nmol/L)	-0.594	0.000**	-0.576	0.000**	0.098	0.458	-0.034	0.796
FAI	0.125	0.342	0.475	0.000**	0.111	0.400	0.224	0.086
Fasting blood glucose (mg/dL)	-0.083	0.532	0.225	0.084	0.306	0.019*	-0.178	0.175
Fasting blood insulin (uIU/mL)	0.969	0.000**	0.855	0.000**	-0.226	0.083	0.314	0.015*
HOMA-IR (%)					-0.202	0.122	0.635	0.063
AMH (ng/mL)	-0.230	0.077	-0.156	0.233	0.317	0.014*	0.194	0.138
Leptin (ng/mL)	0.707	0.000**	0.499	0.000**	-0.278	0.031*	0.123	0.347
Adiponectin (µg/mL)	-0.285	0.028*	-0.365	0.004**	0.349	0.006**	0.010	0.937
Adiponectin/Leptin ratio	-0.642	0.000**	-0.523	0.000**	0.413	0.001**	-0.081	0.541

Note: r=correlation coefficient; BMI=body mass index; WC=waist circumference; WHR=waist to hip ratio; PBF=percent body fat; VFA=visceral fat area; PSF=percent subcutaneous fat; SMM=skeletal muscle mass; HOMA-IR= homeostatic model assessment for insulin resistance; LH=luteinizing hormone; FSH=follicle stimulating hormone; SHBG=sex hormone binding globulin; FAI=free androgen index; FG score=Ferriman Gallwey score. *P<0.05 = significant correlation (2-tailed). **P<0.01 = significant correlation (2-tailed).

DISCUSSION

Studies have revealed that in PCOS patients, metabolic disorders characterized by insulin resistance or hyperinsulinemia and the presence of neuroendocrine disturbances in the form of increased LH levels or LH/FSH ratio are characteristics that are often found along with ovulation disorders, hyperandrogenism, and infertility.[18] An elevated LH/FSH ratio is specifically identified in cases of polycystic ovarian syndrome (PCOS).[19] Furthermore, an association was assumed between adipose tissue and metabolic and neuroendocrine disorders. Depres suggested that visceral obesity might activate the hypothalamus-pituitary-adrenal axis.[18] Adipose tissue, as an endocrine organ, produces adipokines such as leptin and adiponectin, which have been shown to be associated with the occurrence of insulin resistance and metabolic syndrome. Measuring body composition parameters can differentiate fat tissue in the visceral area from other areas, which is more useful in predicting the risk of insulin resistance rather than just measuring BMI.[27] In this study, the focus was on the relationship between parameters of body composition, insulin resistance, levels of leptin and adiponectin, adiponectin/leptin ratio, and LH/FSH ratio in women with PCOS. To our knowledge, this study is the first to investigate the relationship between body composition parameters and the LH/FSH ratio in women with PCOS.

The characteristics of PCOS patients and controls were initially compared. No differences were found in body composition parameters between PCOS patients and controls, contrary to reports from previous studies.[23-25] However, our result was similar to the findings.[28] Furthermore, body composition parameters between obese patients with PCOS and controls, as well as lean PCOS patients and lean controls was not significantly difference. These conflicting results might be due to the different methods of measuring body composition parameters between those studies. The present study used the bioimpedance method, which was indicated to be reliable in measuring body composition parameters.[22] Moreover, the heterogeneity of PCOS pathophysiology and influences of race and environment might contribute to this dissimilarity.

Although body composition did not significantly differ between the two groups, fasting insulin level and HOMA-IR value were higher in women with PCOS, showing enhanced risk of glucose intolerance and insulin resistance in PCOS women. These results were in accordance with other studies.[22,23,29] Based on our study, it is assumed that factors other than biometrics of body composition, such as adipokines, may contribute to insulin resistance in women with PCOS.

Studies have shown a clear association between insulin resistance, glucose intolerance, and disrupted adipokine secretion, particularly adiponectin and leptin, in PCOS-afflicted women.[15,30-32] The current study also uncovered significant differences in adiponectin levels between PCOS and control groups, supporting the notion of insulin resistance due to reduced adiponectin or increased leptin activity. Interestingly, our findings revealed comparable leptin levels across both groups, consistent with earlier studies.[32,33] Adiponectin's role as a potent insulin sensitizer underscores its significance in PCOS-associated insulin resistance. Conversely, leptin, a crucial regulator of energy balance and adiposity, exhibited elevated levels in PCOS women, aligning with prior studies.[7,10,29] Furthermore, the adiponectin/leptin ratio, a key metric, was consistently lower in PCOS cases than controls.[9-11] A parallel study echoed our observations, showing reduced adiponectin levels and no substantial difference in leptin levels in PCOS individuals.[34] This collective evidence underscores the disrupted state of adipokine equilibrium in PCOS, accentuating its association with insulin resistance.

When the coefficient correlation between body composition and HOMA-IR value was investigated, the results found that VFA, which describes visceral fat and PSF as subcutaneous fat markers, positively correlated with HOMA-IR value in both women with PCOS and controls. Similar results also applied to body weight, BMI, and WC. In contrast, SMM, which describes skeletal muscle mass, was negatively correlated with HOMA-IR value in both groups. The results are in accordance with a study that expressed that increasing muscle mass will improve insulin sensitivity and reduce the risk of developing type 2 diabetes.[35]

Moreover, the outcomes revealed intriguing associations: body composition parameters (body weight, BMI, WC, PBF, VFA, and PSF) positively correlated with the LH/FSH ratio, whereas SMM exhibited a negative correlation. Notably, women without PCOS exhibited no such correlations between body composition and the LH/FSH ratio. Supporting our findings, reported a weak negative correlation between body fat percentage and LH in PCOS women but not controls.[23] This implies that although body composition does not substantially differ between PCOS patients and controls, additional variables foster these correlations in PCOS patients. This study pioneers the exploration of body composition's association to the LH/FSH ratio in PCOS women. Furthermore, AMH levels exhibited a positive correlation with the LH/FSH ratio in only PCOS women, aligning with the findings of other studies.[36,37] This could be attributed to the presence of AMH type 2 receptor (AMHR2) in both hypothalamus and pituitary organs.[38]

Moreover, our results showed that leptin levels were negatively correlated with the LH/FSH ratio in women with PCOS but not in controls. These results were in line with a study[16], whereas other studies showed the opposite results.[11,17] The relationship between leptin and LH secretion has been investigated with the conclusion that leptin could affect the hypothalamus and pituitary in the regulation of GnRH pulsatility and LH secretion.[39,40] In addition, the present study found a significant positive correlation between adiponectin levels and the adiponectin/leptin ratio with the LH/FSH ratio in women with PCOS but not in controls. Similar observations were also demonstrated.[14,15] Previous studies demonstrated that adiponectin receptors, Adipor1 and Adipor2, were found on pro-opiomelanocortin (POMC) and neuropeptide Y (NPY) neurons in the arcuate nucleus[41] in addition to being discovered in the anterior pituitary.[42] These outcomes suggest a role for adiponectin in energy homeostasis.

One of the hypotheses of the occurrence of neuroendocrinological disorders in PCOS is the disruption of the sex steroid hormone feedback mechanism in the hypothalamus and pituitary due to exposure to increased androgen levels.[43] However, our study did not show a significant correlation between testosterone levels, FAI, FG scores and LH/FSH ratio in PCOS women or in controls. Other studies have also demonstrated the association of insulin resistance with increased LH and LH/FSH ratio[44,45]; however, this study did not find any significant correlation between both fasting insulin and HOMA-IR.

Interestingly, our study revealed that the LH/

FSH ratio was significantly higher in lean women with PCOS. Conversely, the HOMA-IR value was lower in lean women with PCOS compared to obese women with PCOS. This finding provides further confirmation for the proposed hypothesis, which suggests the existence of two phenotypes of PCOS based on genetic and hormonal analysis. These phenotypes are the 'Reproductive' type, characterized by elevated levels of LH, SHBG, and BMI with relatively low insulin levels, and the 'Metabolic' type, characterized by high BMI, insulin, and glucose levels accompanied by low LH and SHBG.[46] Further investigation is needed to explore this issue. Additionally, the diagnosis and therapeutic approach for these two types of PCOS may vary according to their respective pathophysiology.

Limitations of the present study were the small sample size of both PCOS women and controls recruited from a single center in Indonesia. Therefore, larger studies in populations of diverse backgrounds are required to confirm the results.

CONCLUSION

In conclusion, our study sheds light on the intricate web of metabolic and hormonal interplay in women with PCOS. Through a comprehensive analysis of various factors, this study unraveled a few significant insights. Firstly, there was a nuanced relationship between insulin resistance, adiponectin, and leptin levels in PCOS women. The elevation of HOMA-IR was found to be associated with a decrease in adiponectin, and conversely, an increase in leptin levels. This finding underscores the importance of addressing insulin resistance as a key factor in PCOS-related metabolic alterations. Furthermore, the intricate relationship between AMH and the LH/FSH ratio became evident. Our results indicated that an increase in AMH levels was associated with a higher LH/FSH ratio in PCOS women. This emphasizes the complex influence of hyperandrogenism on the reproductive hormonal balance in PCOS. Notably, we uncovered compelling links between body composition parameters, leptin and adiponectin levels, the adiponectin to leptin ratio, and the LH/FSH ratio in PCOS women. The present study showed that the dysfunction of adipose tissues associated with the dysregulation of adipokines may play a significant role in the mechanism of neuroendocrine disorders in PCOS, which is characterized by an increased LH/FSH ratio and therefore requires further investigation. These associations were not observed in the control group, highlighting the specificity of these interactions to the PCOS population. In summation, our study not only enriches our understanding of the intricate mechanisms underpinning PCOS but also underscores the need for a multifaceted approach when considering therapeutic interventions. As we continue to decipher the pathophysiology of PCOS, our findings offer a steppingstone towards more targeted and effective management strategies for this complex syndrome.

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CONFLICT OF INTEREST

There is no conflict of interests in this paper.

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