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MECHANISMS LINKING INSULIN RESISTANCE TO OVARIAN DYSFUNCTION IN LEAN VERSUS OBESE PHENOTYPES OF POLYCYSTIC OVARY SYNDROME

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in reproductive-aged women and insulin resistance is regarded as central to its reproductive and metabolic abnormalities. The extent to which insulin resistance drives ovarian dysfunction differs between lean and obese phenotypes and this relationship remains incompletely defined among South Asian women. This study aimed to compare metabolic, hormonal and ovarian morphological characteristics between lean and obese women with PCOS and to evaluate the association between insulin resistance and ovarian dysfunction.

Methods: This comparative cross-sectional study was conducted in the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Two hundred fifty women with PCOS were enrolled, comprising 125 lean and 125 obese participants diagnosed on established clinical, biochemical and ultrasonographic grounds. Anthropometric, biochemical, hormonal and ultrasonographic parameters were compared between groups and the homeostasis model assessment of insulin resistance (HOMA-IR) defined insulin resistance status.

Results: Obese participants had significantly higher body mass index, waist circumference, fasting insulin, HOMA-IR androgen levels and an unfavourable lipid profile than lean participants ($p<0.001$ for most variables). Insulin resistance, defined as HOMA-IR of 2.6 or more, was present in 73.6% of obese and 41.6% of lean participants. Ovarian volume, antral follicle count, oligo/anovulation and clinical hyperandrogenism were all significantly more frequent among participants with higher HOMA-IR, regardless of body weight category.

Conclusion: Insulin resistance was strongly and consistently associated with adverse metabolic, hormonal and ovarian features in both lean and obese phenotypes of PCOS, supporting its central pathogenic role independent of body weight.

Keywords: Polycystic ovary syndrome; Insulin resistance; Obesity; HOMA-IR; Ovarian dysfunction

Introduction

Polycystic ovary syndrome (PCOS) is among the most common endocrine and reproductive disorders affecting women of childbearing age, characterised by a combination of chronic anovulation, clinical or biochemical hyperandrogenism and polycystic ovarian morphology [1]. It is now recognised as a disorder with substantial metabolic as well as reproductive consequences, carrying long-term implications for glucose tolerance, lipid metabolism and cardiovascular health [2]. Population-based estimates suggest that PCOS affects approximately 4% to 15% of reproductive-aged women, with prevalence varying according to the diagnostic criteria applied and the population studied [3,4]. Data from South Asian cohorts indicate a comparable, if not higher, burden of the condition, underscoring its relevance to regional clinical practice [5].

The diagnosis of PCOS has been guided since 2003 by the Rotterdam criteria, which require the presence of at least two of three features: oligo-ovulation or anovulation, clinical or biochemical hyperandrogenism and polycystic ovarian morphology on ultrasonography, after exclusion of related endocrinopathies [6,7]. This broadened definition acknowledges the marked clinical heterogeneity of the syndrome, which spans a spectrum from lean, mildly symptomatic women to markedly obese women with pronounced metabolic derangement.

Insulin resistance is now understood to occupy a central position in the pathophysiology of PCOS. Early work demonstrated that insulin resistance in affected women occurs independently of obesity, implicating an intrinsic post-receptor signalling defect rather than adiposity alone [8]. Compensatory hyperinsulinaemia is thought to act on the ovarian theca cells, augmenting androgen biosynthesis and on the pituitary gland, altering gonadotropin secretion, thereby linking metabolic dysfunction directly to reproductive abnormality [9,10]. Obesity, however, is far from an innocent bystander in this process. Excess adiposity, particularly of the visceral pattern, compounds underlying insulin resistance and is present in approximately half of all women diagnosed with PCOS, amplifying both the metabolic and reproductive manifestations of the syndrome [11]. Comparative studies further suggest that the pattern and severity of insulin resistance and its associated clinical expression, may differ across ethnic groups, with South Asian women showing a tendency toward greater insulin resistance at comparatively lower body mass index than their Western counterparts [12].

Despite this growing body of evidence, uncertainty remains regarding how consistently insulin resistance predicts specific reproductive and ovarian abnormalities across the lean and obese phenotypes of PCOS and whether the ovarian and clinical consequences of hyperinsulinaemia are truly phenotype-independent. Because PCOS is associated with long-term risk of impaired glucose tolerance and type 2 diabetes mellitus, an improved understanding of these phenotype-specific mechanisms carries direct clinical relevance for risk stratification and early intervention [13,14]. Much of the existing literature originates from Western populations and comparative data examining insulin resistance and its ovarian correlates across body weight categories in South Asian women remain limited.

This study was therefore designed to compare the clinical, metabolic, hormonal and ovarian morphological characteristics of lean and obese women with PCOS attending a tertiary care center in Bangladesh and to examine the association between insulin resistance, assessed by the homeostasis model assessment of insulin resistance and markers of ovarian dysfunction across the study population, irrespective of body weight phenotype.

Materials and Methods

This comparative cross-sectional study was conducted in the Department of Obstetrics and Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, over a period of thirteen months from June 2009 to July 2010. The study population comprised women of reproductive age diagnosed with polycystic ovary syndrome according to the revised Rotterdam criteria, requiring the presence of at least two of the following three features after exclusion of related endocrinopathies: oligo-ovulation or anovulation, clinical or biochemical hyperandrogenism and polycystic ovarian morphology on transvaginal ultrasonography. A total of 250 eligible women were enrolled by purposive sampling and stratified into two comparable groups of 125 each according to body mass index: a lean group (body mass index less than 23 kg/m²) and an obese group (body mass index of 25 kg/m² or more), in keeping with the Asian body mass index classification. Women with known type 1 or type 2 diabetes mellitus, thyroid dysfunction, hyperprolactinaemia, congenital adrenal hyperplasia androgen-secreting tumours, Cushing syndrome, or those receiving hormonal, insulin-sensitising or ovulation-inducing medication within the preceding three months were excluded, as were women who declined consent. After obtaining informed written consent, a structured proforma was used to record demographic, menstrual and clinical data, including anthropometric measurements of weight, height, body mass index and waist circumference, along with clinical assessment of hirsutism using the modified Ferriman-Gallwey scoring system and examination for acanthosis nigricans. Fasting venous blood samples were collected between the third and fifth day of a spontaneous or progesterone-induced menstrual cycle for estimation of fasting plasma glucose, fasting insulin, lipid profile, total testosterone, sex hormone-binding globulin, luteinising hormone and follicle-stimulating hormone, using standard laboratory assays performed in the hospital biochemistry and endocrinology laboratories. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated from fasting glucose and insulin values, with insulin resistance defined as a value of 2.6 or more. Transvaginal ultrasonography was performed to assess ovarian volume, antral follicle count and stromal echogenicity. Confidentiality of participant information was strictly maintained throughout, with data anonymised prior to analysis to ensure accuracy, reliability and consistency of the dataset. Data were compiled, cross-checked and analysed using Statistical Package for Social Sciences (SPSS) version 16.0. Continuous variables were expressed as mean and standard deviation and compared using the independent samples t-test, while categorical variables were expressed as frequency and percentage and compared using the chi-square test. A p-value of less than 0.05 was considered statistically significant throughout the analysis.

Results

A total of 250 women with PCOS were included in the analysis, comprising 125 lean and 125 obese participants. The two groups were comparable in age and duration of infertility. As expected, BMI and waist circumference were significantly higher among obese participants. A family history of diabetes and acanthosis nigricans were also more frequent in the obese group, whereas the prevalence of primary infertility and hirsutism did not differ significantly between groups (Table 1).

Baseline characteristics

The mean age was 25.8 ± 4.1 years among lean participants and 26.4 ± 4.3 years among obese participants (p=0.264). Mean duration of infertility was 2.6 ± 1.4 and 2.9 ± 1.7 years, respectively (p=0.129). Mean BMI was substantially higher in the obese group than in the lean group (28.4 ± 2.6 vs 21.8 ± 1.2 kg/m²,

p<0.001), as was mean waist circumference (92.8 ± 7.6 vs 74.6 ± 5.2 cm, p<0.001). A family history of diabetes was present in 43.2% of obese participants compared with 30.4% of lean participants (p=0.036). Acanthosis nigricans was considerably more common among obese participants (62.4% vs 17.6%, p<0.001). Primary infertility and hirsutism were observed in 58.4% versus 60.8% (p=0.699) and 53.6% versus 46.4% (p=0.255) of obese and lean participants, respectively (Table 1).

Table 1. Baseline Characteristics of Study Participants (N=250)

Variable	Lean PCOS (n=125)	Obese PCOS (n=125)	p-value
Age (years), mean ± SD	25.8 ± 4.1	26.4 ± 4.3	0.264
BMI (kg/m²), mean ± SD	21.8 ± 1.2	28.4 ± 2.6	<0.001
Waist circumference (cm), mean ± SD	74.6 ± 5.2	92.8 ± 7.6	<0.001
Duration of infertility (years), mean ± SD	2.6 ± 1.4	2.9 ± 1.7	0.129
Primary infertility, n (%)	76 (60.8)	73 (58.4)	0.699
Family history of diabetes, n (%)	38 (30.4)	54 (43.2)	0.036
Acanthosis nigricans, n (%)	22 (17.6)	78 (62.4)	<0.001
Hirsutism (mFG ≥8), n (%)	58 (46.4)	67 (53.6)	0.255

Metabolic and hormonal parameters

Obese participants demonstrated a less favourable metabolic profile than lean participants. Mean fasting plasma glucose was higher in the obese group (5.1 ± 0.7 vs 4.8 ± 0.5 mmol/L, p<0.001), accompanied by higher fasting insulin concentrations (19.8 ± 7.2 vs 12.4 ± 4.6 µU/mL, p<0.001) and HOMA-IR values (4.5 ± 1.9 vs 2.7 ± 1.1, p<0.001). Insulin resistance, defined as HOMA-IR ≥2.6, was present in 73.6% of obese participants compared with 41.6% of lean participants (p<0.001). The obese group also had higher total cholesterol, triglycerides and LDL-cholesterol concentrations, whereas HDL-cholesterol was lower than in the lean group (all p<0.001). Regarding the androgen profile, obese participants had higher total testosterone and free androgen index values and lower SHBG concentrations than lean participants (all p<0.001). LH concentrations were modestly higher among obese participants (10.6 ± 4.4 vs 9.2 ± 3.8 mIU/mL, p=0.009), whereas FSH and the LH/FSH ratio did not differ significantly between groups (p=0.248 and p=0.082, respectively) (Table 2).

Table 2. Metabolic and Hormonal Parameters (N=250)

Parameter		Lean PCOS (n=125), Mean ± SD	Obese PCOS (n=125), Mean ± SD	p-value
Glucose metabolism	Fasting plasma glucose (mmol/L)	4.8 ± 0.5	5.1 ± 0.7	<0.001
	Fasting insulin (µU/mL)	12.4 ± 4.6	19.8 ± 7.2	<0.001
	HOMA-IR	2.7 ± 1.1	4.5 ± 1.9	<0.001

	HOMA-IR ≥2.6, n (%)	52 (41.6)	92 (73.6)	<0.001
Lipid profile	Total cholesterol (mmol/L)	4.4 ± 0.7	4.9 ± 0.9	<0.001
	Triglycerides (mmol/L)	1.2 ± 0.4	1.6 ± 0.6	<0.001
	LDL-cholesterol (mmol/L)	2.6 ± 0.6	3.1 ± 0.8	<0.001
	HDL-cholesterol (mmol/L)	1.2 ± 0.2	1.0 ± 0.2	<0.001
Androgen profile	Total testosterone (ng/mL)	0.62 ± 0.21	0.74 ± 0.26	<0.001
	Free androgen index	7.8 ± 3.2	11.4 ± 4.6	<0.001
	SHBG (nmol/L)	48.6 ± 16.4	36.2 ± 12.8	<0.001
Gonadotropins	LH (mIU/mL)	9.2 ± 3.8	10.6 ± 4.4	0.009
	FSH (mIU/mL)	6.0 ± 1.9	6.3 ± 2.1	0.248
	LH/FSH ratio	1.62 ± 0.68	1.78 ± 0.74	0.082

Ovarian morphology and menstrual patterns

Ovarian morphological parameters differed significantly between the two phenotypes. Mean ovarian volume was greater among obese participants than lean participants (11.8 ± 3.4 vs 9.4 ± 2.2 mL, p<0.001). Ovarian volume >10 mL was present in 65.6% of obese participants compared with 35.2% of lean participants (p<0.001). Similarly, mean antral follicle count was higher in the obese group (17.2 ± 5.4 vs 13.6 ± 4.2 follicles per ovary, p<0.001) and AFC ≥12 was more frequent among obese participants (75.2% vs 54.4%, p=0.001). Increased stromal echogenicity was also more common in the obese group (71.2% vs 51.2%, p=0.001). Menstrual abnormalities were common in both groups. Oligomenorrhea was present in 70.4% of obese and 65.6% of lean participants (p=0.418), while amenorrhea occurred in 15.2% and 12.8%, respectively (p=0.584). Regular menstrual cycles were reported by 14.4% of obese participants and 21.6% of lean participants (p=0.142). Overall, the distribution of menstrual patterns did not differ significantly between the two groups (Table 3).

Table 3. Ovarian Morphological Parameters and Menstrual Patterns (N=250)

Parameter		**Lean PCOS (n=125), Mean ± SD/ n (%)**	**Obese PCOS (n=125), Mean ± SD/ n (%)**	**p-value**
Ultrasound findings	Mean ovarian volume (mL)	9.4 ± 2.2	11.8 ± 3.4	<0.001
	Ovarian volume >10 mL	44 (35.2)	82 (65.6)	<0.001
	Antral follicle count (per ovary)	13.6 ± 4.2	17.2 ± 5.4	<0.001
	AFC ≥12	68 (54.4)	94 (75.2)	0.001
	Increased stromal echogenicity	64 (51.2)	89 (71.2)	0.001

Menstrual patterns	Oligomenorrhe	82 (65.6)	88 (70.4)	0.418
	Amenorrhea	16 (12.8)	19 (15.2)	0.584
	Regular cycles	27 (21.6)	18 (14.4)	0.142

Association between insulin resistance and ovarian dysfunction

Across the entire study population, 106 participants had HOMA-IR <2.6 and 144 had HOMA-IR ≥2.6. Markers of ovarian dysfunction were more frequent among participants with higher HOMA-IR. Ovarian volume >10 mL was observed in 66.7% of participants with HOMA-IR ≥2.6 compared with 28.3% of those with HOMA-IR <2.6 (p<0.001). Similarly, AFC ≥12 was more frequent among participants with HOMA-IR ≥2.6 (72.2% vs 54.7%, p=0.004). Oligo/anovulation, defined as oligomenorrhea or amenorrhea, was present in 86.8% of participants with HOMA-IR ≥2.6 compared with 75.5% of those with HOMA-IR <2.6 (p=0.021). Clinical hyperandrogenism was also more frequent in the higher HOMA-IR group (61.8% vs 45.3%, p=0.009) (Table 4). These findings indicate that greater insulin resistance was associated with several clinical and ovarian features of PCOS, although the cross-sectional design does not establish a temporal or causal relationship.

Table 4. Relationship Between Insulin Resistance and Ovarian Dysfunction (N=250)

Outcome	HOMA-IR	Lean PCOS	Obese PCOS	Overall (N=250)	p-value
Ovarian volume >10 mL	<2.6	14/73 (19.2%)	16/33 (48.5%)	30/106 (28.3%)	<0.001
	≥2.6	30/52 (57.7%)	66/92 (71.7%)	96/144 (66.7%)	
AFC ≥12	<2.6	36/73 (49.3%)	22/33 (66.7%)	58/106 (54.7%)	0.004
	≥2.6	32/52 (61.5%)	72/92 (78.3%)	104/144 (72.2%)	
Oligo/anovulation	<2.6	54/73 (74.0%)	26/33 (78.8%)	80/106 (75.5%)	0.021
	≥2.6	44/52 (84.6%)	81/92 (88.0%)	125/144 (86.8%)	
Clinical hyperandrogenism	<2.6	32/73 (43.8%)	16/33 (48.5%)	48/106 (45.3%)	0.009
	≥2.6	26/52 (50.0%)	63/92 (68.5%)	89/144 (61.8%)	

Discussion

The present study compared lean and obese phenotypes of polycystic ovary syndrome and examined how insulin resistance relates to ovarian dysfunction across these groups. The two groups were similar in age and duration of infertility, indicating that the comparison largely isolated the effect of body weight, consistent with the traditional characterisation of PCOS as a syndrome with a shared reproductive core

but a variable metabolic overlay [1]. As anticipated, obese participants had substantially higher body mass index and waist circumference than lean participants and this anthropometric divergence was accompanied by a markedly less favourable metabolic profile, including higher fasting insulin, higher HOMA-IR and a greater prevalence of insulin resistance. This pattern mirrors the well-established observation that adiposity, particularly central adiposity, compounds the underlying insulin resistance of PCOS rather than acting as its sole cause [11]. Notably, insulin resistance was present in a substantial proportion of lean participants as well, supporting the view that insulin resistance in PCOS is not simply a consequence of excess weight but reflects an intrinsic abnormality of insulin action that can occur independently of obesity [8]. Dunaif's early clamp-based studies first demonstrated this phenomenon and later work extended the concept by proposing a post-binding defect in insulin receptor signalling as the likely mechanistic basis [9].

The HOMA-IR threshold applied in this study to define insulin resistance is consistent with cut-off values validated in earlier work using the same homeostasis model assessment approach in women with PCOS [15,16] and the underlying HOMA-IR methodology itself remains a widely accepted, practical alternative to more labour-intensive clamp techniques in large clinical studies [15]. The observation that acanthosis nigricans was considerably more frequent among obese participants aligns with earlier reports describing acanthosis nigricans as a recognisable cutaneous marker of underlying insulin resistance and compensatory hyperinsulinaemia in women with PCOS [17], reinforcing its utility as a low-cost bedside clue to metabolic risk, particularly relevant in resource-limited settings such as ours.

The androgen and gonadotropin findings in the present study broadly reflect the mechanistic link between hyperinsulinaemia and ovarian androgen excess described in earlier work, in which insulin was shown to directly stimulate thecal androgen biosynthesis and to potentiate luteinising hormone action on the ovary [10]. Obese participants in this study had higher total testosterone, higher free androgen index and lower sex hormone-binding globulin than lean participants, a pattern consistent with the recognised suppressive effect of hyperinsulinaemia on hepatic sex hormone-binding globulin synthesis, which in turn increases the bioavailable androgen fraction [18]. The modestly higher luteinising hormone concentration observed among obese participants, without a corresponding difference in follicle-stimulating hormone or in the luteinising hormone to follicle-stimulating hormone ratio, suggests that gonadotropin disturbance in this cohort was comparatively subtle relative to the more pronounced metabolic and androgenic differences between phenotypes. Hirsutism, graded using the modified Ferriman-Gallwey scoring method that remains the standard clinical tool for quantifying terminal hair growth [19], did not differ significantly between lean and obese participants, suggesting that clinical hyperandrogenism in this cohort was not simply a function of body weight but reflected a broader androgenic disturbance common to both phenotypes.

Ovarian morphological findings showed that obese participants had significantly greater ovarian volume and antral follicle count than lean participants, findings that are consistent with international consensus criteria describing increased ovarian volume and follicle number as core ultrasonographic features of polycystic ovarian morphology [20]. Importantly, when the analysis moved beyond simple phenotype comparison to examine insulin resistance directly, ovarian volume greater than 10 mL, antral follicle count of 12 or more, oligo/anovulation and clinical hyperandrogenism were all significantly more common among participants with higher HOMA-IR, a pattern observed consistently within both lean and obese subgroups. This cross-phenotype consistency strengthens the inference that insulin resistance itself,

rather than adiposity per se, is closely linked to ovarian dysfunction in PCOS, a relationship previously highlighted in populations where insulin resistance appears more pronounced at comparatively lower body mass index, including South Asian cohorts [12]. Given the well-documented long-term risk of impaired glucose tolerance and type 2 diabetes mellitus associated with insulin resistance in PCOS [13,14], these findings support assessing insulin resistance in all women with PCOS, including those of normal body weight, rather than reserving metabolic screening for obese patients alone, allowing earlier identification of women at heightened long-term risk who might otherwise be overlooked on the basis of body habitus [2].

Limitations and Recommendations

This study was conducted at a single tertiary care center, which may limit generalisability of the findings to the wider community and its cross-sectional design precludes any conclusion about the temporal or causal relationship between insulin resistance and ovarian dysfunction. The use of surrogate insulin resistance indices rather than the euglycaemic clamp technique and the absence of long-term follow-up, are further limitations. Larger, multicenter, prospective studies incorporating longitudinal follow-up are recommended to confirm these findings and to clarify the temporal relationship between insulin resistance and ovarian dysfunction across PCOS phenotypes and routine insulin resistance screening should be considered for both lean and obese women with PCOS in clinical practice.

Conclusion

Insulin resistance was highly prevalent in both lean and obese phenotypes of polycystic ovary syndrome and was consistently associated with adverse ovarian, hormonal and metabolic features across the study population. Obesity amplified but did not solely determine this relationship, as insulin resistance independently predicted ovarian dysfunction irrespective of body weight. These findings underscore the importance of assessing insulin resistance in all women with PCOS, regardless of phenotype, to guide timely metabolic and reproductive risk stratification.

References

1. Franks S. Polycystic ovary syndrome. N Engl J Med. 1995;333(13):853-861.
2. Ehrmann DA. Polycystic ovary syndrome. N Engl J Med. 2005;352(12):1223-1236.
3. Knochenhauer ES, Key TJ, Kahsar-Miller M, Waggoner W, Boots LR, Azziz R. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: a prospective study. J Clin Endocrinol Metab. 1998;83(9):3078-3082.
4. Ramezani Tehrani F, Simbar M, Tohidi M, Hosseinpanah F, Azizi F. The prevalence of polycystic ovary syndrome in a community sample of Iranian population: Iranian PCOS prevalence study. Reprod Biol Endocrinol. 2011;9:39.
5. Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. J Pediatr Adolesc Gynecol. 2011;24(4):223-227.
6. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Fertil Steril. 2004;81(1):19-25.
7. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41-47.

8. Dunaif A, Segal KR, Futterweit W, Dobrjansky A. Profound peripheral insulin resistance, independent of obesity, in polycystic ovary syndrome. Diabetes. 1989;38(9):1165-1174.
9. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. Endocr Rev. 1997;18(6):774-800.
10. Nestler JE, Jakubowicz DJ, de Vargas AF, Brik C, Quintero N, Medina F. Insulin stimulates testosterone biosynthesis by human thecal cells from women with polycystic ovary syndrome by activating its own receptor and using inositolglycan mediators as the signal transduction system. J Clin Endocrinol Metab. 1998;83(6):2001-2005.
11. Gambineri A, Pelusi C, Vicennati V, Pagotto U, Pasquali R. Obesity and the polycystic ovary syndrome. Int J Obes Relat Metab Disord. 2002;26(7):883-896.
12. Wijeyaratne CN, Balen AH, Barth JH, Belchetz PE. Clinical manifestations and insulin resistance (IR) in polycystic ovary syndrome (PCOS) among South Asians and Caucasians: is there a difference? Clin Endocrinol (Oxf). 2002;57(3):343-350.
13. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet. 2007;370(9588):685-697.
14. Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. J Clin Endocrinol Metab. 1999;84(1):165-169.
15. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-419.
16. DeUgarte CM, Bartolucci AA, Azziz R. Prevalence of insulin resistance in the polycystic ovary syndrome using the homeostasis model assessment. Fertil Steril. 2005;83(5):1454-1460.
17. Panidis D, Skiadopoulos S, Rousso D, Ioannides D, Panidou E. Association of acanthosis nigricans with insulin resistance in patients with polycystic ovary syndrome. Br J Dermatol. 1995;132(6):936-941.
18. Vermeulen A, Verdonck L, Kaufman JM. A critical evaluation of simple methods for the estimation of free testosterone in serum. J Clin Endocrinol Metab. 1999;84(10):3666-3672.
19. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab. 1961;21:1440-1447.
20. Balen AH, Laven JS, Tan SL, Dewailly D. Ultrasound assessment of the polycystic ovary: international consensus definitions. Hum Reprod Update. 2003;9(6):505-514.