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Original Research Article

Prediction of metabolic syndrome by visceral adiposity index, lipid accumulation product and model of adiposity index amongst infertile women with and without polycystic ovary syndrome

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ABSTRACT

Background: This study was conducted to compare visceral adiposity index (VAI), lipid accumulation product (LAP) and model of adiposity index (MAOD) for prediction of metabolic syndrome (MS) amongst infertile women with and without PCOS.
Methods: It was a case control, retrospective study performed in gynecology outpatient department of a tertiary care center. Total 143 infertile women with PCOS and 367 infertile women without PCOS were recruited in the study. Waist circumference (WC), BMI, waist hip ratio (WHR), insulin resistance, VAI, LAP, MOAD were assessed in both groups.
Results: Significantly higher values of WC, WHR, systolic BP, insulin postprandial and all 3 adiposity indices were found among infertile women with PCOS as compared to women without PCOS. In hormonal profile, testosterone, AMH, FSH, prolactin, estradiol was found to be significantly higher in PCOS group. For predicting MS in PCOS women, VAI had the highest AUC 0.878 with a cut off value of 3.1, highest sensitivity of 88.9%, specificity of 90.7%, positive and negative predictive value of 76.2% and 96% respectively followed by LAP and MOAD.
Conclusions: To conclude, all three adiposity indexes VAI, LAP and MOAD were significantly raised in PCOS women. VAI followed by LAP were the best indicators to predict metabolic syndrome in women with PCOS.

Keywords: LAP, Metabolic syndrome, MOAD, PCOS, VAI

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders, affecting 5-10% of the population in women of reproductive age.[1,2] It is characterized by hyperandrogenemia, chronic anovulation, and polycystic ovary morphology. Diagnosis is made according to Rotterdam criteria which requires presence of two of three: oligomenorrhea, clinical or biochemical hyperandrogenism, polycystic ovarian appearance on ultrasonography (≥12 follicles measuring 2-9 mm in at least one ovary and/or increased ovarian volume, >10 ml).

Insulin resistance plays a key role in the pathophysiology of PCOS and leads to development of metabolic aberrations including central obesity, glucose intolerance, type 2 diabetes, dyslipidaemia, hypertension and coronary artery disease.[3,4] Central obesity, also measured by an increased waist circumference (WC) and waist-to-hip ratio, is considered as a precise predictor of obesity-related metabolic abnormalities. It has replaced body mass index (BMI) for defining a clinical diagnosis of metabolic syndrome.[5] An increased WC and fasting triglycerides (TG) reflect the inability of a woman to manage and store extra energy in subcutaneous fat depots. Therefore, hypertriglyceridemic waist phenotype points to visceral adiposity which is further associated with various metabolic abnormalities. Visceral adiposity and PCOS interact to induce premature atherosclerosis and amplified cardiovascular morbidity by mechanisms which include

low grade chronic inflammation, metabolism of sex steroids and cortisol in visceral fat, and the secretion of adipokines such as leptin, which exert direct effects on the ovary.[6,7]

The androgen excess and PCOS (AE-PCOS) society has recommended the assessment of cardiometabolic risk in women with PCOS in clinical practice.[8] Therefore, the assessment of visceral adiposity should be performed independent of overall obesity to screen for cardiovascular morbidity and may be useful in the therapeutic intervention for PCOS.

Magnetic resonance imaging (MRI) or computed tomography (CT) are suggested as the "gold standard methods" for assessing the degree of visceral adipose tissue but they are not practical in routine clinical practice due to limited availability, high cost and associated risk of radiation exposure.

Visceral adiposity index (VAI), lipid accumulation product (LAP) and model of adiposity index (MOAD) are 3 novel visceral adiposity indexes, proposed for the evaluation of cardiometabolic risk in adult population.

Indian population has higher visceral obesity and insulin resistance as compared to Caucasians. Considering scanty evidence available for Indian women so far, we aimed to examine if simple adiposity indices like VAI, LAP and MOAD can be useful to predict metabolic syndrome in Indian infertile women with and without PCOS. The present study would also compare and determine the best predictor out of these 3 for diagnosing metabolic syndrome.

METHODS

This case control, retrospective study was a part of a survey sponsored by the department of science and technology done for evaluating causes of infertility in a tertiary care hospital. Women between the age group of 18-40 years presenting to gynecology outpatient department were recruited after obtaining written informed consent to participate in the survey. This study was initiated after approval from the ethics committee of human research of the Institute. The present study included 510 infertile women among which 143 were diagnosed as PCOS and 367 were without PCOS.

Inclusion criteria included female patients with polycystic ovary syndrome (diagnosed according to the Rotterdam criteria which require the presence of two of three: oligomenorrhea (less than 6-9 menses per year), clinical or biochemical hyperandrogenism and polycystic ovary appearance on ultrasonography i.e. having ≥12 follicles measuring 2-9 mm in at least one ovary and/or increased ovarian volume, >10 ml after exclusion of other pathologies like congenital adrenal hyperplasia, hyperprolactinemia, diabetes mellitus.[9,10]

BMI was calculated from body weight and height by the standard formula: BMI = (weight in kg/height in m^2). Individuals with a BMI ≥25 kg/m^2 were considered as overweight.[11] Waist-hip ratio ≥ 0.80 cm was considered to having central obesity.[12] Blood pressure ≥130/80 mmHg was considered to be abnormal.

Visceral adiposity index (VAI) and lipid accumulation product (LAP), model of adiposity index (MOAD) were calculated using the proposed formula:

VAI = WC/36.58 + (one.89 × BMI) × TG/0.81 × 1.52/HDL.

LAP = (waist (cm) - 58) × TG Concentration (mmol/L)

MOAD = WC / [36.58 + (1.89 × BMI)]

Metabolic syndrome 13 was diagnosed if 3 values from following 5 were present: 1) fasting blood sugar >5.6 mmol/l (100 mg/dl), 2) blood pressure > 130/80 mmHg, 3) triglyceride > 1.7 mmol/l (150 mg/dl), 4) HDL<1.04 mmol/l (40 mg/dl), 5) waist circumference >80 cm.

Clinical investigations

Thorough history including menstrual, obstetrics, personal, past, family, treatment details and complete physical examination was done for all patients.

Blood collection was done after overnight fasting of 10-12 hours and sample was analysed for fasting lipid profile, OGTT, serum insulin and hormonal profile on day 2, 3 of menstrual cycle. Lipid profile was considered to be abnormal if cholesterol >200 mg/dl, triglycerides ≥1.7 mmol/l (150 mg/dl). HDL≤1.04 mmol/l (40 mg/dl). Lipid profile was estimated by using enzymatic colorimetric technique and for metabolic syndrome NCEP-ATP III guidelines were followed.[13]

Blood sugar values were determined during a 75g oral glucose tolerance test (OGTT) and were assessed according to WHO criteria.[14] Presence of insulin resistance was recognized if the woman had impaired fasting glucose, impaired or deranged glucose tolerance, HbA1c of 5.7 to 6.4% or postprandial insulin ≥41 µU/ml or HOMA IR>2.5. Hormonal profile included FSH, LH, estradiol, total testosterone, prolactin and TSH on day 2 or 3 of menstrual cycle and serum progesterone was measured at day 21-23 of menstrual cycle. Hormonal estimation was done by chemiluminescence immunoassay. Transvaginal ultrasound scan of ovaries on 2nd day of cycle was done by using the 5MHz transvaginal transducer by an experienced sonographer.[15]

Statistical analysis was done using SPSS 16.0. Student's t test and Chi square test were used to compare categorical variables; Mann Whitney test was used for non-parametric data. Receiver operating characteristic (ROC) curve analysis was employed to determine the clinical efficacy

and optimal cut-off values for lipid ratios in predicting MS. P value <0.05 was considered significant.

RESULTS

Total subjects included in the study were 510, with PCOS 143 and 367 without PCOS. Table 1 compared clinical and metabolic profile of infertile women with and without PCOS.

Women with and without PCOS had comparable age and BMI but the waist-hip ratio, waist circumference, systolic BP and post glucose insulin were significantly higher in women with PCOS.

Table 1: Comparison of clinical and metabolic profile of infertile women with and without PCOS.

Variables	PCOS (N=143)	Without PCOS (N=367)	P value
Age (years)	26 (25-30)	25 (50-75)	0.476
BMI (kg/m^2)	24.2 (21.67-28.44)	23.63 (21.64-26.67)	0.12
WHR	0.83 (0.82-0.88)	0.83 (0.77-0.87)	0.004
WC (CM)	78.74 (76.2-86.4)	76.2 (68-84)	<0.001
SBP (mmHg)	116 (112-120)	120 (112-128)	0.015
DBP (mmHg)	76 (70-78)	72 (68-80)	0.205
FBS (mmol/l)	5.33 (5-5.67)	5.28 (4.78-5.78)	0.598
PPBS (mg/dl)	134 (120-140)	130 (115-140)	0.401
Insulin fasting (µU/ml)	10.2 (7.3-18.6)	10.8 (6.4-15)	0.087
Insulin post glucose µU/ml	43.9 (23.4-90)	25.1 (20-40)	<0.001

Table 2: Comparison of lipid profile of infertile women with and without PCOS.

Variables	PCOS (N=143)	Without PCOS (N=367)	P value
Triglycerides (mmol/l)	1.40 (1.19-1.81)	1.19 (0.80-1.55)	<0.001
Cholesterol (mg/dl)	180 (150-200)	160 (135-180)	<0.001
HDL (mmol/l)	1.034 (0.98-1.11)	1.034 (0.93-1.11)	0.234

Table 3: Comparison of hormonal profile of infertile women with and without PCOS.

Variables	PCOS (N=143)	Non PCOS (N=367)	P value
LH (IU/L)	7.99 (4.42-11.1)	6.46 (4.44-10.4)	0.266
Testosterone	34 (18.8-42)	20.9 (2-40.15)	<0.001
TSH	2.5 (1.59-4.13)	2.227 (1.50-3.87)	0.108
AMH	14.52 (11.64-16.65)	0.913 (0.63-2.01)	<0.001
FSH	6.12 (5.03-8.41)	8.2 (6.2-10.31)	<0.001
Estradiol	51.35(43.46-80.42)	22.32 (4.88-44.43)	<0.001
Prolactin	15.5 (11-24.29)	11.67 (8.03-18.16)	<0.001

Table 4: Adiposity indices of infertile women with and without PCOS.

Adiposity Index	PCOS (N=143)	Non PCOS (N=367)	P value
VAI	2.499 (2.04-3.31)	2.05 (1.42-2.71)	<0.001
LAP	29.35 (22.24-29.35)	19.85 (10.53-32.20)	<0.001
MOAD	0.95 (0.92-1.004)	0.93 (0.85-1.01)	0.003

Table 5: Comparison of adiposity indexes that best predict metabolic syndrome.

Adiposity index	Cutoff values for predicting MS	AUC	SS%	SP%	PPV%	NPV%
VAI	3.12	0.878	88.9	90.7	76.2	96
LAP	39.52	0.873	86.1	85	66	94.8
MOAD	1.01	0.480	36.1	79.4	37.1	78.7

Table 2 compares lipid profile of infertile women with and without PCOS. Triglycerides and total cholesterol were significantly higher in the women with PCOS.

Table 3 depicts hormonal profile of infertile women with and without PCOS. Serum testosterone, AMH, FSH, estradiol and prolactin were significantly higher in women with PCOS.

Table 4 compares adiposity index of infertile women with and without PCOS. All the three adiposity indices were significantly higher in PCOS women.

By considering NCEP-ATP III guidelines, magnitude of metabolic syndrome was found to be 18.88% (27/143 patients) in PCOS patients and 5.1% (19/367 patients) in women without PCOS.

Figure 1 and Table 5 compares adiposity indexes that best predict metabolic syndrome.

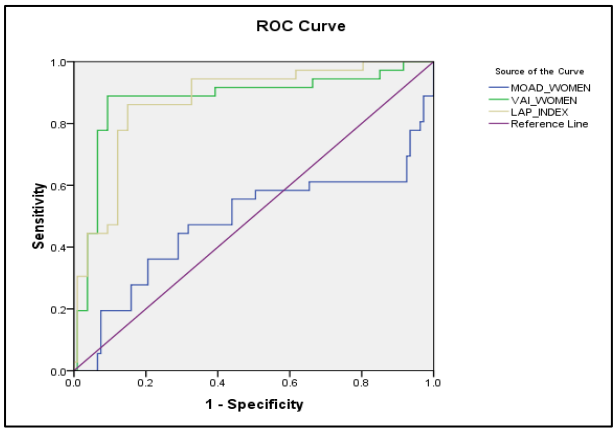

Figure 1: ROC of comparison of adiposity indexes that best predict metabolic syndrome.

VAI had the highest AUC 0.878 with a cut off value of 3.12, highest sensitivity of 88.9%, specificity of 90.7%, positive and negative predictive value of 76.2% and 96% respectively followed by LAP and MOAD. For predicting metabolic syndrome in PCOS women, VAI was found to be the best predictor with highest AUC, sensitivity, specificity, positive and negative predictive value followed by LAP and MOAD as shown in Figure 1 and Table 5.

DISCUSSION

Obesity, diabetes, hypertension and coronary artery disease have become important and leading cause of death globally. Early screening and timely treatment of individuals with visceral adiposity is very important in reducing long tern morbidity and mortality associated with metabolic syndrome. VAI, LAP and MOAD are adiposity indices suggested as simple, practical and low-cost tools for the estimation of cardiometabolic dysfunction associated with visceral adiposity. The optimal cut-off values of VAI, LAP and MOAD for predicting metabolic syndrome have not been thoroughly investigated in Indian women with PCOS. In this study, we assessed whether the VAI, LAP and MOAD could be used as markers for detecting metabolic syndrome in Indian women with and without PCOS. Application of these indices may replace the need to use multiple, complex and expensive investigations and may recognize women who require lifestyle changes or pharmacologic interventions to prevent or manage metabolic syndrome.

In this study, although cases and controls were matched according to age and BMI, women with PCOS had significantly higher waist circumference and waist hip ratio as compared to women without PCOS which points towards central or visceral obesity. Systolic blood pressure and postprandial insulin level, marker for insulin resistance were also significantly higher in PCOS women than in women without PCOS (p value <0.001). A study conducted in South India also reported significant association of metabolic syndrome in women with PCOS with age ≥25 years or with central obesity.[16] Body fat distribution which is in android pattern may be the result as well as the cause of hyperandrogenism. It ultimately sets up vicious cycle of hyperandrogenism, central adiposity, hyperinsulinemia and metabolic syndrome.[17]

According to hormonal profile, the values for testosterone, AMH, FSH, estradiol and prolactin were significantly high for PCOS women as compared to non PCOS women (p value <0.001). Triglyceride and cholesterol levels were high in women with PCOS than non PCOS women with p value <0.001.

Although the age and BMI of women with and without PCOS was comparable, all 3 adiposity indices VAI, MOAD, LAP index were significantly higher in PCOS women as compared to those without PCOS (<0.001, 0.003, <0.001 respectively).

Metabolic syndrome was significantly higher in women with PCOS (18.88%) than non-PCOS women (5.1%). Other studies had also shown PCOS and obesity are associated with insulin resistance and compensatory hyperinsulinemia. Insulin has direct action on ovary to stimulate the biosynthesis of testosterone and it results in disturbance of other hormones like AMH, FHS, estradiol and serum prolactin.[18]

In a study performed on one hundred ninety three PCOS patients VAI showed significant correlation with body weight, fasting glucose, free testosterone, estradiol, total cholesterol, V-GT, SGPT, homeostasis mode assessment and anovulation.[19]

Another study compared various adiposity indexes in PCOS women with normo-ovulatory non hirsute women concluded that LAP has sensitivity of 88% and positive predictive value of 98% for screening of cardiometabolic complications. Another best predictor of metabolic

syndrome is waist circumference (83% sensitivity and 97% PPV) and VAI (81% sensitivity and 95% PPV). [20]

There are few other studies which have shown that visceral adiposity index is a predictor of metabolic syndrome, adverse cardiac events, diabetes, anovulation and hyperandrogenism in PCOS women. It is also a predictor of insulin resistance and hyperinsulinemia.[20]

A study performed in young PCOS women compared LAP and VAI with total cholesterol/HDL-cholesterol reported that both LAP and VAI were effective markers to assess metabolic disturbances, high insulin resistance and dyslipidemia (cut -off value of lipid accumulation product 18.24, sensitivity 81.43%, specificity 73.49% with PPV 75.0% and NPV: 77.27%) similarly visceral adiposity index with cut off value 2.19 (sensitivity 81.16%, specificity 72.15%, PPV 74.65% and NPV 72.22%).[21] Similar results have been observed in other studies.[22,23]

In the present study, VAI was found to be the best predictor of metabolic syndrome in PCOS women with highest AUC 0.878 followed by LAP and MOAD AUC 0.873, 0.480 respectively. Metabolic syndrome is further responsible for various cardio metabolic risks. However, in other studies on PCOS, MOAD and VAI were not found to be superior to WHR and BMI as far as correlation with derangement of sex hormones and metabolic syndrome is concerned.[24]

CONCLUSION

To conclude, in clinical and metabolic profile, WHR, WC, SBP, Insulin post glucose, triglyceride and cholesterol were found to be significantly higher in PCOS group (p value <0.05). In hormonal profile testosterone, AMH, FSH, prolactin, estradiol were found to be significantly higher in PCOS group.

All three adiposity indexes VAI, LAP and MOAD were significantly raised in PCOS women. VAI and LAP can be used to detect metabolic syndrome. VAI followed by LAP were the best indicator to predict metabolic syndrome in women with PCOS.

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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Androgen Excess Society. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. J Clin Endocrinol Metab. 2006;91(11):4237-45.
2. Asuncion M, Calvo RM, San Millan JL. A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. J Clin Endocrinol Metab. 2000;85:2434-8.
3. Escobar-Morreale HF, San Millan JL. Abdominal adiposity and the polycystic ovary syndrome. Trends Endocrinol Metab 2007;18:266-272.
4. Ormazabal V, Nair S., Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. Cardiovasc Diabetol. 2018;17:122.
5. Zimmet P, Magliano D, Matsuzawa Y, Alberti G, Shaw J. The metabolic syndrome: a global public health problem and a new definition. J Atheroscler Thromb. 2005;12:295-300.
6. Wild S, Pierpoint T, McKeigue P, Jacobs H. Cardiovascular disease in women with polycystic ovary syndrome at long-term follow-up: a retrospective cohort study. Clin Endocrinol. 2000;52:595-600.
7. Shaw LJ, Bairey Merz CN, Azziz R, Stanczyk FZ, Sopko G, Braunstein GD, et al. Withdrawn: postmenopausal women with a history of irregular menses and elevated androgen measurements at high risk for worsening cardiovascular event-free survival: results from the National Institutes of Health-National heart, lung, and blood institute sponsored women's ischemia syndrome evaluation. J Clin Endocrinol Metab. 2008;93(4):1276-84.
8. Wild RA, Carmina E, Diamanti-Kandarakis E, Dokras A, Escobar-Morreale HF, Futterweit W, et al. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the androgen excess and polycystic ovary syndrome (AE-PCOS) Society. J Clin Endocrinol Metab. 2010;95(5):2038-49.
9. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab. 1961;21:1440-7.
10. The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and longterm health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19:41-7.
11. Strauss JF. Some new thoughts on the pathophysiology and genetics of polycystic ovarian syndrome. Ann New York Acad Sci. 2003;997(1):42-8.
12. De Leo V, Musacchio MC, Palermo V, Di Sabatino A, Morgante G, Petraglia F. Polycystic ovary syndrome and metabolic co-morbidities: therapeutic options. Drugs Today. 2009;45:763-75.
13. Redmond GP, Bergfeld WF. Diagnostic approach to androgen disorders in women: acne, hirsutism and alopecia. Cleve Clin J Med. 1990;57(5):423-7.
14. Dokras A, Bochner M, Hollinrake E, Markham S, Vanvoorhis B, Jagasia DH. Screening women with polycystic ovary syndrome for metabolic syndrome. Obstet Gynecol. 2005;106:1317.

15. Saxena P, Prakash A, Nigam A, Mishra A. Polycystic ovary syndrome: a clinical, hormonal, and metabolic assessment in relation to body mass index. Indian J Endocrinol Metab. 2012;16(6).
16. Mandrelle K, Kamath MS, Bondu DJ, Chandy A. Prevalence of metabolic syndrome in women with polycystic ovary syndrome attending an infertility clinic in a tertiary care hospital in south India. J Hum Reprod Sci. 2012;5(1):26-31.
17. Barber TM, McCarthy MI, Wass JA, Franks S. Obesity and polycystic ovary syndrome. Clin Endocrinol. 2006;65:137-45.
18. Hirschberg AL. Polycystic ovary syndrome, obesity and reproductive implications. Women Health. 2009;5(5):529-40.
19. Androulakis I, Kandaraki E, Christakou C, Karachalios A, Marinakis E, Paterakis T, et al. Visceral adiposity index (VAI) is related to the severity of anovulation and other clinical features in women with polycystic ovary syndrome. Clin Endocrinol. 2014;81(3):426-31.
20. Tehrani FR, Minooee S, Azizi F. Comparison of various adiposity indexes in women with polycystic ovary syndrome and normo-ovulatory non-hirsute women: a population-based study. Eur J Endocrinol. 2014;171(2):199-207.
21. Zheng SH, Li XL. Visceral adiposity index as a predictor of clinical severity and therapeutic outcome of PCOS. Gynecol Endocrinol. 2016;32(3):177-83.
22. Adanas G, Özgen G. The relation of visceral adiposity index and lipid accumulation product with metabolic, anthropometric, and hormonal parameters in patients with polycystic ovary syndrome. J Surg Med. 2020;4(8):664-8.
23. Abruzzese GA, Cerrrone GE, Gamez JM, Graffigna MN, Belli S, Lioy G, et al. Lipid accumulation product (LAP) and visceral adiposity index (VAI) as markers of insulin resistance and metabolic associated disturbances in young Argentine women with polycystic ovary syndrome. Metab Res. 2017;49(1):23-9.
24. Borruel S, Molto JF, Alpanes M, Fernandez-Duran E, Alvarez-Blasco F, Luque-Ramirez M, et al. Surrogate markers of visceral adiposity in young adults: waist circumference and body mass index are more accurate than waist hip ratio, model of adipose distribution and visceral adiposity index. PloS One. 2014;9(12):e114112.

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