Original Article

Access this article online
Quick Response Code:

Website: www.jehp.net
DOI: 10.4103/jehp.jehp_1605_22

Visceral adiposity index and lipid accumulation product index: The promising role in assessing cardiometabolic risk in non-obese patients of PCOS

Aritri Bir, Arindam Ghosh, Sourav Chowdhury[1]

Department of Biochemistry, Dr. B.C. Roy Multispeciality Medical Research Centre, IIT Kharagpur, West Bengal, India, [1]Apollo Multispeciality Hospital, Kolkata, West Bengal, India

Address for correspondence:
Dr. Arindam Ghosh, Department of Biochemistry, Dr. B.C. Roy Multispeciality Medical Research Centre, IIT Kharagpur, West Midnapore, West Bengal - 721 302, India.
E-mail: drghosh.arindam@gmail.com; arindam@bcrmrc.iitkgp.ac.in

Received: 08-11-2022
Accepted: 05-12-2022
Published: 31-05-2023

Abstract:

BACKGROUND: The combination of metabolic disorders like obesity, insulin resistance, reduced glucose tolerance, diabetes mellitus, and dyslipidemia poses an increased risk of cardiovascular events in patients with PCOS which is closely related to increased visceral fat accumulation. This study explored the noninvasive adiposity markers like Visceral Adiposity Index (VAI) and Lipid Accumulation Product (LAP) levels in non-obese PCOS patients and their associations with clinico-metabolic parameters.

METHODS AND MATERIALS: The case–control study was conducted with a total of 66 PCOS cases and 40 healthy controls (aged 18–35). Their lipid profile, fasting insulin levels and homeostatic model of insulin resistance index, VAI, and LAP scores were estimated. The cases were divided into three groups depending on the presence of cardiovascular risk factors. The predictive power of LAP and VAI with respect to cardiovascular outcomes was assessed by ROC curves.

RESULTS: The VAI and LAP scores have shown a significant positive correlation with markers of metabolic syndrome. When multiple risk factors are considered simultaneously, the cutoff value of VAI is 2.59 with 91% sensitivity and 80% specificity, and that of the LAP score is 40.2 with 91% sensitivity and 83% specificity. The area under curves for VAI was 0.935 and for LAP was 0.945 considering the presence of at least three risk factors.

CONCLUSION: The study concluded that with a definitive cutoff value, VAI and LAP were inexpensive, simple, and effective screening tools for cardiometabolic risk assessment in non-obese women with PCOS and can be an effective way to determine long-term cardiovascular outcomes and prevent them.

Keywords:

Cardiometabolic risk, Lipid Accumulation Product, Metabolic syndrome, Non-obese PCOS, Visceral Adiposity Index

Introduction

Polycystic ovary syndrome (PCOS), or Stein–Leventhal syndrome, is a common endocrine disorder in women of reproductive age group with a worldwide prevalence of 4–20%.[1,2] According to the Rotterdam criteria, PCOS is commonly defined by two of the following three features: (i) oligo-ovulation or anovulation, (ii) clinical and/or biochemical signs of hyperandrogenism, or (iii) polycystic ovaries, once related endocrinological and gynecological disorders have been excluded.[3] PCOS is reported to be associated with multiple metabolic derangements like obesity, insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus, and dyslipidemia.[4-6] In addition to these,

How to cite this article: Bir A, Ghosh A, Chowdhury S. Visceral adiposity index and lipid accumulation product index: The promising role in assessing cardiometabolic risk in non-obese patients of PCOS. J Edu Health Promot 2023;12:148.

numerous studies have shown that cardiovascular morbidity and mortality are higher in patients with polycystic ovary syndrome (PCOS) compared with age-matched controls.[7,8] The clustering of metabolic disturbances poses a higher risk of developing cardiovascular events in PCOS patients.

Of late, categorical anthropometric and biochemical assessments in PCOS patients have been given much importance. Multiple studies showing the presence of insulin resistance in both lean and obese women with PCOS have suggested that obesity is not necessarily an expression of cardiometabolic risk.[9,10] Studies have identified a subset of metabolically healthy obese (MHO) individuals having a beneficial metabolic profile with high insulin sensitivity, normotension, and favorable lipid profile.[11,12] On the other hand, another subset of normal-weight individuals with adverse metabolic parameters has been mentioned as metabolically unhealthy non-obese (MUNO).[13] It has been predicted that increased accumulation of visceral fat in comparison with lesser peripheral fat distribution can be a possibility for conversion of MHO subjects to metabolically unhealthy obese (MUO) state.[14] This necessitates identifying some other more specific markers of adiposity and distinguishing metabolically unhealthy polycystic ovary syndrome (MU-PCOS) from metabolically healthy PCOS (MH-PCOS) which serves as the aim of this present study.

Computerized tomography (CT) or magnetic resonance imaging (MRI), in this context, has been recommended as significant screening tool to measure visceral adiposity.[15] However, these methods are too costly and cumbersome to be used in routine clinical practice.

VAI has been proven to be a valuable indicator for the assessment of visceral adipose tissue and its function.[16] Various population studies have shown a successful association with the severity of many metabolic dysfunctions.[16,17]

The Lipid Accumulation Product (LAP), side by side, is an index based on two components, waist circumference (WC) and triglyceride (TG) concentration, and was designed to indicate the risk of cardiovascular disease.[18] As the LAP score shares two of the five components of metabolic syndrome, it has been found to be a reliable tool to detect metabolic syndrome as well.[18,19]

Although these indices have been correlated with conditions like hyperlipidemia and metabolic syndrome, there is no study that investigates their role as a screening tool in non-obese PCOS patients to assess the cardiometabolic risk. Hence in the present study, we aimed for a systematic investigation into VAI and LAP levels as superior body adiposity markers and their correlations with clinico-metabolic parameters in overweight and/or obese, and non-obese PCOS patients to determine whether any definitive value can be pinpointed to use them as a screening tool for assessment of cardiometabolic risks.

Materials and methods

Study design and setting

This case–control study was conducted with women with PCOS (as per Rotterdam criteria) attending the gynecology outpatient department at a tertiary care medical college and hospital in the city of Durgapur, West Bengal, India.[3] Age-matched healthy controls were chosen from the accompanying patients' relatives attending the gynecology outpatient department.

Study participants and sampling

The women with PCOS and the controls belonged to the reproductive age group (18–35 years). The controls were eumenorrheic with no hirsutism and no family history of PCOS. A purposive sampling technique was followed for the study.

Exclusion criteria:

The patients who were provisionally enrolled for the study were further scrutinized and excluded from the final study if they had any one of the following exclusion criteria, namely,

1. PCOS patients taking any cholesterol-lowering drugs
2. Patients' BMI of more than 23
3. Women treated with clomiphene citrate, oral contraceptives, antiandrogens, or insulin-sensitizing drugs during the six months prior to the first examination

After consideration of exclusion criteria, 66 non-obese PCOS cases were found eligible for our present study. Forty age-matched healthy women were selected as controls.

Data collection tool and technique

All participants underwent comprehensive medical assessment including detailed medical history, physical examination, and anthropometric measurements like height, body weight, waist circumference, and hip circumference according to standardized procedures. Waist circumference was measured at the midpoint between the lower rib margin and the top of the iliac crest at the end of exhalation. Hip circumference was measured at the level of the greater trochanter. Body Mass Index (BMI) was calculated as body weight (kg) divided by the square of height in meters. According to

WHO Asian criteria of BMI, overweight was defined as 23 ≤ BMI <28, and obesity as BMI ≥28.[20] Waist/Hip ratio (WHR) was calculated as waist circumstance divided by hip circumstance. The non-obese PCOS cases were then analyzed on the basis of the presence or absence of one or more cardiometabolic risk factors like WC >80 cm, hypertension (SBP >130 mm of Hg), triglyceride >150 mg/dl, HDL <50 mg/dl FBS >100 mg/dl and were categorized into no risk, low risk (at least one risk factor), moderate risk (at least two risk factors), and high risk (three or more risk factors).

Biochemical assays

After overnight fasting, blood samples were drawn from the antecubital veins between the third and fifth days of the natural menstrual cycle or progestin-withdrawal bleeding when the patient had amenorrhea. The measurement of fasting plasma glucose, Total Cholesterol (TC), Low-Density Lipoprotein Cholesterol (LDL-C), High-Density Lipoprotein Cholesterol (HDL-C), and triglycerides (TGs) were done in Siemens Dimension Chemiluminescence clinical chemistry analyzer with the help of commercially available kits (Siemens). Quality control validation was done using commercially available control serum from Bio-Rad. The analysis of serum estradiol, progesterone, testosterone, Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), and fasting insulin levels was done in ELISA method using commercially available ELISA Kits (Invitrogen) using automated ELISA Reader (Tecan Sunrise) and automated ELISA Washer (ERBA Transasia). Homeostasis model assessment of insulin resistance (HOMA-IR) index was calculated using the formula insulin (μIU/ml)×glucose (mmol/l)/22.5.[21] IR was defined as HOMA-IR >2.77.[22]

VAI was determined by following gender-specific formula for women:

[WC (cm)/(36.58 + (1.89 × BMI))] × (TG (mmol/l)/0.81) × (1.52/HDL-C (mmol/l)).[17,18]

LAP was calculated as [WC (cm) – 58] × TG (mmol/l) in women.[21]

Ethical consideration

Participants were informed of the purpose of the study and given the opportunity to provide written consent. All participants received assurance that their data would be kept private, that taking part in the study was entirely up to them, and that they could discontinue at any time. If participants had any comments, criticisms, or information regarding any issues, they could get in touch with the researcher. Ethical clearance was obtained from the institutional ethics committee prior to commencing the study [Ref No. IQMC/IEC/LTR/17/02/28 (07)].

Statistical analysis

Statistical analysis was performed using SPSS version 20.0 (IBM, Armonk, New York, USA). Continuous variables were presented as Mean ± Standard Deviation (SD) except for skewed variables, which were represented as medians (interquartile ranges). Differences between groups were performed by one-way ANOVAs. Comparisons between categorical variables were performed by the Chi-square (χ^2) test. Physical activity levels, TG, FPG, fasting insulin, HOMA-IR, WHR, VAI, and LAP were logarithmically transformed before analysis due to non-normal distribution. The area under the receiver operating characteristic curve (AUC) with 95% confidence intervals was used to assess the discriminative ability of adiposity measurements on diabetes and insulin resistance. A nonparametric approach was used to compare the AUC of various anthropometric measures. We used the optimal operating point with a minimum sensitivity of 80%. All statistical tests were two-sided, and a P value <0.05 was considered statistically significant.

Results

A total of 106 individuals participated in the study. Among them, 66 were non-obese patients suffering from polycystic ovarian disease, while 40 were age-matched healthy controls. Body Mass Index (BMI), waist circumference (WC), Waist/Hip Ratio (WHR), Systolic and diastolic Blood pressure (SBP and DBP), Serum Triglycerides (TG), Total Cholesterol (TC), High-Density Lipoprotein (HDL), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Fasting Blood Glucose (FBG), Fasting serum Insulin and Insulin Resistance (HOMA-IR) were measured in both the cases and controls. A comparative chart of these parameters is shown in Table 1 with the statistical analysis of Mean, Standard Deviation, and Standard Error of the Mean along with the statistical significance of the comparison of means (P value)

The non-obese PCOS cases were analyzed on the basis of the presence or absence of one or more cardiometabolic risk factors like WC >80 cm, hypertension (SBP >130 mm of Hg), triglyceride >150 mg/dl, HDL <50 mg/dl FBS >100 mg/dl and were categorized into no risk, low risk (at least one risk factor), moderate risk (at least two risk factors), and high risk (three or more risk factors). The comparison of the various parameters among these subgroups is shown in Table 2. The VAI and LAP scores for all three subgroups were calculated using the standard formula. The data are shown in Table 2. Pearson correlation of cardiometabolic risk factors and the risk indices, i.e., Visceral Adiposity Index and Lipid Accumulation Product score, was done.

Table 1: Statistical analysis of metabolic parameters in cases and control subjects

	Case and controls	Mean	Standard deviation	SEM	*P*
WC (cms)	Control	94.16	1.56	0.31	<0.001
	PCOS case	80.54	3.02	0.36	
BMI	Control	20.17	2.84	0.56	0.384
	PCOS case	20.64	2.11	0.25	
TG (mg/dl)	Control	91.70	22.92	4.58	<0.001
	PCOS case	144.64	9.19	1.09	
HDL (mg/dl)	Control	48.94	10.90	2.18	0.041
	PCOS case	52.56	5.85	0.69	
WHR	Control	0.85	0.002	0.0005	0.003
	PCOS case	0.852	0.003	0.0004	
SBP (mm of Hg)	Control	112	5	1.08	0.002
	PCOS case	121	15	1.87	
DBP (mm of Hg)	Control	72	5	1.07	0.038
	PCOS case	76	8	1.03	
TC (mg/dl)	Control	151.91	9.64	1.92	<0.001
	PCOS case	168.95	18.88	2.25	
FBG (mg/dl)	Control	82.83	8.53	1.70	<0.001
	PCOS case	98.14	15.46	1.84	
LH	Control	8.72	2.48	0.49	<0.001
	PCOS case	12.14	3.79	0.45	
FSH	Control	6.93	2.09	0.41	0.002
	PCOS case	5.38	1.47	0.17	
Insulin	Control	6.29	2.03	0.40	<0.001
	PCOS case	12.51	6.50	0.77	

BMI=Body mass index, WC=Waist circumference, WHR=Waist/Hip Ratio, SBP and DBP=Systolic and Diastolic blood pressure, TG=Serum triglycerides, TC=Total cholesterol, HDL=High-density lipoprotein, FSH=Follicle-stimulating hormone, LH=Luteinizing hormone, FBG=Fasting blood glucose, SEM=Standard error of the mean

Table 2: Subdivisions of PCOS cases according to cardiometabolic risks

	No-risk		Mild risk		Moderate risk		High risk	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
WC	77.91	1.16	81.11	2.99	81.07	3.16	83.20	1.68
BMI	20.34	1.99	19.93	1.75	20.65	1.95	22.31	2.38
TG	140.38	6.74	140.30	5.14	144.63	7.73	158.99	4.57
HDL	55.46	3.02	55.18	4.23	51.07	6.90	45.62	3.24
WHR	0.85	0.003	0.85	0.003	0.85	0.003	0.85	0.003
SBP	107.77	5.97	115.75	15.96	131.32	12.05	136.58	3.72
DBP	69.57	7.16	74.05	9.45	79.60	6.48	82.83	3.46
TC	161.14	8.84	166.63	18.73	163.58	8.32	193.92	23.23
FBG	91.56	7.52	90.52	7.43	97.38	14.33	122.93	11.58
LH	12.19	3.69	12.38	3.87	12.08	3.88	11.73	4.13
FSH	5.35	1.39	5.48	1.55	5.27	1.50	5.40	1.58
Insulin	12.67	6.30	12.57	6.30	12.52	6.48	12.14	7.95
HOMA-IR	2.45	1.64	2.31	1.67	2.53	1.67	2.50	1.77
VAI	2.23	0.15	2.36	0.17	2.62	0.38	3.14	0.28
LAP score	31.56	2.10	36.68	5.15	37.55	4.42	45.25	3.44

BMI=Body mass index, WC=waist circumference, WHR=Waist/Hip ratio, SBP and DBP=Systolic and Diastolic blood pressure, TG=Serum triglycerides, TC=Total cholesterol, HDL=High-density lipoprotein, FSH=Follicle-stimulating hormone, LH=Luteinizing hormone, FBG=Fasting blood glucose, HOMA-IR=Homeostasis model assessment-estimated insulin resistance, VAI=Visceral adiposity index, LAP=Lipid accumulation product

ROC curve and area under the curve were calculated by plotting sensitivity against 1-specificity for both VAI and LAP with respect to the presence of cardiometabolic risk factors mentioned in Table 2. To get a precise idea regarding the cutoff points of the above-mentioned indices with respect to the existing indices of cardiometabolic risk factors, we calculated the ROC and AUC analysis multiple times with respect to the presence of one or more risk factors. First, we calculated the ROC and AUC of LAP and VAI with the presence of only one risk factor (WC >80 cm, or hypertension (SBP >130 mm of Hg) or TG >150 mg/dl or HDL <50 mg/dl or FBG >100 mg/dl). Then, the same was calculated with the presence of at least two risk factors and then in patients with at least three or more risk factors. The curves are shown in Figure 1.

The area under curves of the ROC analysis and the cutoff points for sensitivity and 1-specificity are tabulated in Table 3. From Figure 1 and Table 3, we can see that depending on a number of risk factors we get a cutoff value of both VAI and LAP. The statistical plot and its analysis show the best results when multiple risk factors are considered simultaneously with the cutoff value of the Visceral Adiposity Index being 2.59 with 91% sensitivity and 80% specificity and that of Lipid Accumulation Product score being 40.2 with 91% sensitivity and 83% specificity. The area under curves for VAI was 0.935 and for LAP was 0.945 considering the presence of at least three risk factors.

Discussion

The myriad of metabolic derangements poses a great threat of cardiovascular risk in women with PCOS. The pool of studies has already shown a strong association of metabolic syndrome in PCOS cases.[23,24] Insulin resistance (IR) is an independent risk factor for cardiovascular disease (CVD), and central body fat accumulation also contributes to the same.[25,26] PCOS, therefore, is itself considered a metabolic disorder featuring both of them. It appears from various studies that the form of adiposity in women with PCOS differs. PCOS patients, irrespective of obesity, have a greater propensity to accumulate fat in the upper part of the body when compared to control subjects matched for weight or BMI.[27,28] Therefore, following the consensus statement of the Androgen Excess Society for routine screening of BMI, waist circumference (WC), serum lipid/glucose, and blood pressure is of immense value for the prevention of cardiometabolic disease in these women.[29] The conventional anthropometric indices like BMI, WC, WHR, and WHtR have been, however, documented inefficiently due to their failure in characterizing proper body fat distribution.[30-33] BMI has poor precision being gender and ethnicity

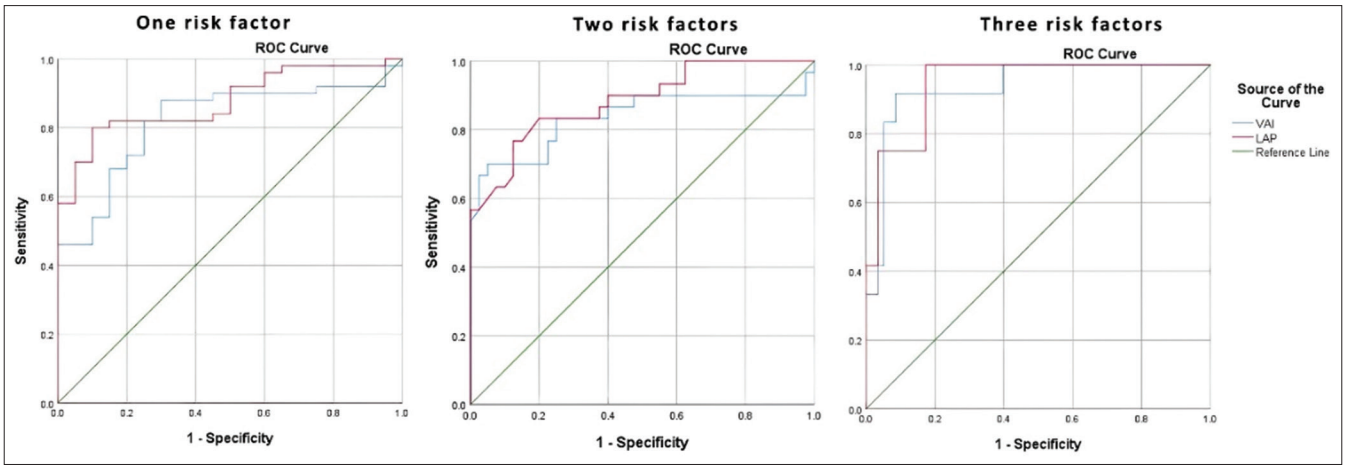

Figure 1: ROC Curves of LAP and VAI with respect to the presence of cardiometabolic risk factors.

Table 3: Comparative analysis of AUC and cutoff scores of VAI and LAP along with their sensitivity and specificity values

Test result variable (s)	Number of risk factors	Area under curve	Cutoff points	Cutoff sensitivity (%)	Cutoff specificity (%)
Visceral adiposity index	3 risk factors	0.935	2.59	91	80
	2 risk factors	0.836	2.40	83	75
	1 risk factor	0.819	2.25	82	75
Lipid accumulation product score	3 risk factors	0.945	40.2	91	83
	2 risk factors	0.883	35.4	80	70
	1 risk factor	0.876	32.9	82	80

nonspecific.[34] WC, another widely used index, shows a poor correlation in non-obese PCOS patients.[33] Since people with different body heights have the same WC, they are unlikely to have the same chance of metabolic abnormalities.

The LAP index and VAI, on the other hand, are two of the available adiposity complex indicators that show promise for predicting cardiometabolic events in both normal and PCOS women.[16,18,35,36] The LAP index is more efficient since it expresses both anatomic and physiological changes related to lipid overaccumulation.[37] The VAI is also a marker of altered adipocytokine content, reduced lipolytic activity, and increased plasma-free fatty acids in women with PCOS because it contains both physical (BMI and WC) and metabolic (TG and HDL) parameters.[35,38] The VAI has been shown to be one of the best predictors of MetS in a normal population by Knowles *et al*.,[39] which corroborates our findings. In patients with PCOS, Wiltgen *et al*. and Amato *et al*. considered the LAP index and VAI to be accurate and accessible indicators of cardiovascular risk.[16,36,38] Furthermore, in support of our study, Kahn stated that the LAP index value is more accurate than the BMI in predicting metabolic disturbances.[23]

However, to contradict our observations, Wildman *et al*.[12] found that the WC and BMI were equivalent in predicting CVD in normal subjects. Vazquez *et al*.[40] found that the BMI, WHR, and WC had similar potential in predicting type 2 diabetes. These differences may be due to genetic factors, lifestyle traits, and dietary patterns, in addition to the various criteria used to diagnose MetS or PCOS. Another contributing factor may be the lower BMI of our PCOS subjects compared to those in other studies. Finally, the approach used to recruit PCOS and control subjects may have a major impact on assessing cardiometabolic risks.

Overall, when comparing women with PCOS to women with no androgen abundance, the acceptable adiposity indicators and their optimum cutoff values differ. Even the euglycemic hyperinsulinemic clamping method, the gold standard to identify IR, is costly and time-consuming, and indexes that depend on FPG are similarly difficult to obtain. The VAI and LAP indices are a simple metric that can be used in everyday clinical practice and demographic trials to measure cardiometabolic risk associated with visceral adiposity as a proxy predictor of visceral adipose tissue dysfunction resulting in dyslipidemia and insulin resistance, but with a different threshold in different groups.

The strengths of the study include a unique study population of non-obese PCOS patients who have been further stratified using the presence of one or more risk factors. This stratification can help to understand the role of VAI and LAP with existing cardiovascular risk factors in early identification and lifestyle modification to alter the state of morbidity and mortality outcomes in the short and long term. This study, however, has some limitations. First, other machine-based measurements of visceral adiposities, such as computed tomography or dual-energy X-ray absorptiometry, were not used to verify the VAI's function in assessing visceral adiposity

in PCOS patients. Secondly, there is a possible drawback in that we used the HOMA-IR as a surrogate marker for insulin resistance assessment. Despite the fact that the HOMA-IR and gold standard clamp methods have a strong correlation, it may be inaccurate in PCOS. Thirdly, since the current study was focused on a single-center cohort in a region of Eastern India, further research in multiple centers or with different ethnic groups is required to establish the relationship. Furthermore, our research has a limitation in that we lacked sufficient power to sub-analyze our data in order to compare the adiposity indexes of different phenotypes of PCOS women.

The study concluded that the VAI and LAP were simple and effective tools for cardiometabolic risk assessment in non-obese women with PCOS and can be an effective way to screen and determine long-term cardiovascular outcomes. However, further studies are needed to extrapolate the indices in clinical management. That being said there is a wide scope of our findings in this study and if sufficiently replicated using wide population-based studies using multiple ethnic cohorts, that data thus achieved can be used to construct simple mobile applications. It can be based on this cutoff criteria where patients can input certain risk factors as selectable and the result based on the outcome can be represented in an alarming graphical way which can create mass awareness. It is indeed a form of evidence-based medicine and will certainly help in health promotion through very early detection and effective and timely intervention of cardiovascular accidents in high-risk and susceptible populations.

Conclusion

It can be concluded that our study is the first of its kind to identify definitive cutoff values of parameters Visceral Adiposity Index and Lipid Accumulation Product score based on the presence of certain risk factors in non-obese PCOS patients, which can be easily used as a screening tool for creating awareness among patients and individuals as a motivation for lifestyle modification and start medication. It can also serve as a tool for general physicians especially in the peripheral and remote areas in decision making prior to referral of patients to super specialists. VAI and LAP could be used to recognize the risk of cardiovascular incidences in metabolic syndrome in individuals with non-obese PCOS who, in addition to their counterparts with obesity along with PCOS, also require lifestyle changes and counseling.

Acknowledgement

The authors acknowledge the involvement of non-teaching staff of the Gynecology Outpatient department, IQ City Medical College, and the Hospital for their support in sample collection as well as assisting in anthropometric measurements. The support of laboratory personnel in the biochemical analysis is also acknowledged. In addition, the authors acknowledge the input of the Institutional Ethics and Research committee to refine the technical aspects of the study.

Abbreviations used: Polycystic ovary syndrome (PCOS), Body Mass Index (BMI), waist circumference (WC), Waist/Hip Ratio (WHR), Systolic and diastolic Blood pressure (SBP and DBP), Serum Triglycerides (TG), Total Cholesterol (TC), High-Density Lipoprotein (HDL), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Fasting Blood Glucose (FBG) homeostasis model assessment-estimated insulin resistance (HOMA-IR), Visceral Adiposity Index (VAI), Lipid Accumulation Product (LAP), Standard Deviation (SD)

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Deswal R, Narwal V, Dang A, Pundir CS. The prevalence of polycystic ovary syndrome: A brief systematic review. J Hum Reprod Sci 2020;13:261–71.
2. Nahidi F, Tehrani FR, Ghodsi D, Jafari M, Majd HA, Abdolahian S. The effectiveness of lifestyle training program promoting adolescent health with polycystic ovarian syndrome: A study protocol for a randomized controlled study. J Edu Health Promot 2021;10:351.
3. 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;19:41–7.
4. Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. Diabetes Care 1999;22:141–6.
5. Yildiz BO, Knochenhauer ES, Azziz R. Impact of obesity on the risk for polycystic ovary syndrome. J Clin Endocrinol Metab 2008;93:162–8.
6. Tehrani HG, Allahdadian M, Zarre F, Ranjbar H, Allahdadian F. Effect of green tea on metabolic and hormonal aspect of polycystic ovarian syndrome in overweight and obese women suffering from polycystic ovarian syndrome: A clinical trial. J Edu Health

Promot 2017;6:36.
7. Zhao L, Zhu Z, Lou H, Zhu G, Huang W, Zhang S, *et al*. Polycystic ovary syndrome (PCOS) and the risk of coronary heart disease (CHD): A meta-analysis. Oncotarge 2016;7:33715–21.
8. de Groot PC, Dekkers OM, Romijn JA, Dieben SW, Helmerhorst FM. PCOS, coronary heart disease, stroke and the influence of obesity: A systematic review and meta-analysis. Hum Reprod Update 2011;17:495–500.
9. Cree-Green M, Rahat H, Newcomer BR, Bergman BC, Brown MS, Coe GV, *et al*. Insulin Resistance, hyperinsulinemia, and mitochondria dysfunction in nonobese girls with polycystic ovarian syndrome. J Endocr Soc 2017;1:931–44.
10. Toosy S, Sodi R, Pappachan JM. Lean polycystic ovary syndrome (PCOS): An evidence-based practical approach. J Diabetes Metab Disord 2018;17:277–85.
11. Stefan N, Kantartzis K, Machann J, Schick F, Thamer C, Rittig K, *et al*. Identification and characterization of metabolically benign obesity in humans. Arch Intern Med 2008;168:1609–16.
12. Wildman RP, Muntner P, Reynolds K, McGinn AP, Rajpathak S, Wylie-Rosett J, *et al*. The obese without cardiometabolic risk factor clustering and the normal weight with cardiometabolic risk factor clustering: Prevalence and correlates of 2 phenotypes among the US population (NHANES 1999–2004). Arch Intern Med 2008;168:1617–24.
13. Mathew H, Farr OM, Mantzoros CS. Metabolic health and weight: Understanding metabolically unhealthy normal weight or metabolically healthy obese patients. Metabolism 2016;65:73–80.
14. Hwang YC, Hayashi T, Fujimoto WY, Kahn SE, Leonetti DL, McNeely MJ, *et al*. Visceral abdominal fat accumulation predicts the conversion of metabolically healthy obese subjects to an unhealthy phenotype. Int J Obes (Lond) 2015;39:1365–70.
15. Klopfenstein BJ, Kim MS, Krisky CM, Szumowski J, Rooney WD, Purnell JQ. Comparison of 3 T MRI and CT for the measurement of visceral and subcutaneous adipose tissue in humans. Br J Radiol 2012;85:e826–30.
16. Amato MC, Giordano C, Galia M, Criscimanna A, Vitabile S, Midiri M, *et al*. Visceral Adiposity Index: A reliable indicator of visceral fat function associated with cardiometabolic risk. Diabetes Care 2010;33:920–2.
17. Bozorgmanesh M, Hadaegh F, Azizi F. Predictive performance of the visceral adiposity index for a visceral adiposity-related risk: Type 2 diabetes. Lipids Health Dis 2011;10:88.
18. Kahn HS. The "lipid accumulation product" performs better than the body mass index for recognizing cardiovascular risk: A population-based comparison. BMC Cardiovasc Disord 2005;5:26.
19. Taverna MJ, Martínez-Larrad MT, Frechtel GD, Serrano-Ríos M. Lipid accumulation product: A powerful marker of metabolic syndrome in healthy population. Eur J Endocrinol 2011;164:559–67.
20. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet 2004;363:157–63.
21. Gutch M, Kumar S, Razi SM, Gupta KK, Gupta A. Assessment of insulin sensitivity/resistance. Indian J Endocrinol Metab 2015;19:160–4.
22. Svendsen PF, Nilas L, Nørgaard K, Jensen JE, Madsbad S. Obesity, body composition and metabolic disturbances in polycystic ovary syndrome. Hum Reprod 2008;23:2113–21.
23. Ehrmann DA, Liljenquist DR, Kasza K, Azziz R, Legro RS, Ghazzi MN, *et al*. Prevalence and predictors of the metabolic syndrome in women with polycystic ovary syndrome. J Clin Endocrinol Metab 2006;91:48–53.
24. Ding T, Hardiman PJ, Petersen I, Wang FF, Qu F, Baio G. The prevalence of polycystic ovary syndrome in reproductive aged women of different ethnicity: A systematic review and meta-analysis. Oncotarget 2017;31:2841–55.
25. Balkau B, Eschwège E. Insulin resistance: An independent risk factor for cardiovascular disease? Diabetes Obes Metab 1999;1(Suppl 1):S23–31.
26. Carmina E, Bucchieri S, Esposito A, Del Puente A, Mansueto P, Orio F, *et al*. Abdominal fat quantity and distribution in women with polycystic ovary syndrome and extent of its relation to insulin resistance. J Clin Endocrinol Metab 2007;92:2500–5.
27. Kirchengast S, Huber J. Body composition characteristics, sex hormone levels and circadian gonadotropin fluctuations in infertile young women. Coll Antropol 1999;23:407–23.
28. Yucel A, Noyan V, Sagsoz N. The association of serum androgens and insulin resistance with fat distribution in polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol 2006;126:81–6.
29. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, *et al*. The androgen excess and PCOS society criteria for the polycystic ovary syndrome: The complete task force report. Fertil Steril 2009;91:456–88.
30. Elagizi A, Kachur S, Lavie CJ, Carbone S, Pandey A, Ortega FB, *et al*. An overview and update on obesity and the obesity paradox in cardiovascular diseases. Prog Cardiovasc Dis 2018;61:142–50.
31. Ross R, Neeland IJ, Yamashita S, Shai I, Seidell J, Magni P, *et al*. Waist circumference as a vital sign in clinical practice: A Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. Nat Rev Endocrinol 2020;16:177–89.
32. Khoury M, Manlhiot C, McCrindle BW. Role of the waist/height ratio in the cardiometabolic risk assessment of children classified by body mass index. J Am Coll Cardiol 2013;62:742–51.
33. Després JP, Lemieux I, Bergeron J, Pibarot P, Mathieu P, Larose E, *et al*. Abdominal obesity and the metabolic syndrome: Contribution to global cardiometabolic risk. Arterioscler Thromb Vasc Biol 2008;28:1039–49.
34. Wang L, Southerland J, Wang K, Bailey BA, Alamian A, Stevens MA, *et al*. Ethnic differences in risk factors for obesity among adults in California, the United States. J Obes 2017;2017:2427483.
35. Zheng SH, Li XL. Visceral adiposity index as a predictor of clinical severity and therapeutic outcome of PCOS. Gynecol Endocrinol 2016;32:177–83.
36. Wiltgen D, Benedetto IG, Mastella LS, Spritzer PM. Lipid accumulation product index: A reliable marker of cardiovascular risk in polycystic ovary syndrome. Hum Reprod 2009;24:1726–31.
37. Xia C, Li R, Zhang S, Gong L, Ren W, Wang Z, *et al*. Lipid accumulation product is a powerful index for recognizing insulin resistance in non-diabetic individuals. Eur J Clin Nutr 2012;66:1035–8.
38. Amato MC, Pizzolanti G, Torregrossa V, Misiano G, Milano S, Giordano C. Visceral adiposity index (VAI) is predictive of an altered adipokine profile in patients with type 2 diabetes. PLoS One 2014;9:e91969.
39. Knowles KM, Paiva LL, Sanchez SE, Revilla L, Lopez T, Yasuda MB, *et al*. Waist circumference, body mass index, and other measures of adiposity in predicting cardiovascular disease risk factors among Peruvian adults. Int J Hypertens 2011;2011:931402.
40. Vazquez G, Duval S, Jacobs DR Jr, Silventoinen K. Comparison of body mass index, waist circumference, and Waist/Hip ratio in predicting incident diabetes: A meta-analysis. Epidemiol Rev 2007;29:115–28.