Background: Cardiovascular disease (CVD) is one of the debilitating consequences of polycystic ovary syndrome (PCOS). Early diagnosis of metabolic syndrome (MetS) with a simple but accurate method can reduce the risk of progression to CVD in PCOS. Aims: This study aimed to determine the accuracy of various anthropometric indices and lipid accumulation product (LAP), in assessing the risk of MetS in PCOS. Settings and Design: This is a cross-sectional study including 150 PCOS women and 100 control subjects. Materials and Methods: Anthropometric parameters were measured and calculated. Lipid profile, fasting plasma glucose (FPG), and insulin were estimated. MetS was detected according to the International Diabetes Federation criteria. Statistical Analysis: Logistic regression and receiver operating characteristic curve analysis were applied to determine the potential association of anthropometric indices such as body mass index, waist circumference (WC), waist-to-hip ratio, waist-to-height ratio, conicity index (CI), visceral adiposity index (VAI), abdominal volume index (AVI), body adiposity index (BAI), and a body shape index (ABSI) and LAP with MetS. Results: In our study of PCOS women of the south Indian population, the prevalence of MetS was 59.3%, which was higher than other populations and the cutoff values of V AI and LAP were 6.05 and 53, respectively. V AI showed the strongest association with MetS, followed by diastolic blood pressure BP, FPG, and LAP. Conclusions: We recommend V AI and LAP as new indices for MetS diagnosis. As these indices exhibit population specificity, it is imperative that independent cutoffs are determined for every demographic population.

Keywords: Anthropometric indices, lipid accumulation product, metabolic syndrome, polycystic ovary syndrome, visceral adiposity index

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most frequent causes of infertility in women of childbearing or reproductive age. It is mainly characterised by irregularity in the menstrual cycle, obesity, hyperandrogenism, and polycystic ovary.¹ The worldwide prevalence of PCOS lies between 5% and 26% depending on the population and diagnostic criteria applied.²,³ PCOS patients might show metabolic consequences such as insulin resistance, Type 2 diabetes, obesity, dyslipidemia, and hyperinsulinemia. These form the risk factors of metabolic syndrome (MetS) and therefore, increase the susceptibility of those women of developing cardiovascular disease (CVD).⁴ Several studies proved...
that women with PCOS have an increased tendency of developing obesity, especially visceral obesity and lipid abnormalities during reproductive age.\cite{5,7} Adiposity has a significant role in maintaining and generating PCOS.\cite{8}

Body mass index (BMI) assesses the total obesity of PCOS patients,\cite{9} but BMI cannot estimate abdominal fat distribution. It seems intra-abdominal fat has a stronger association with the risk of obesity-related morbidity than overall adiposity.\cite{10} Hence, additional anthropometric indices such as elevated waist circumference (WC), waist-to-hip ratio (WHR), and waist-to-height ratio (WHR) are being used to measure central obesity.\cite{11} Related epidemiological studies expressed that these measurements were strongly correlated with MetS [Table 1]. As presented in Table 1, some studies in different populations showed that the visceral adiposity index (VAI) is another index that could be used as an indicator of MetS and cardiometabolic risk. A body shape index (ABSI), abdominal volume index (AVI), conicity index (CI), and body adiposity index (BAI) were the other anthropometric indices which showed correlation with MetS and CVD parameters such as dysfunction of glucose metabolism and central obesity.\cite{11,27} All of the above anthropometric methods are simple, noninvasive, cost-effective, and do not require any special training.\cite{25} However, an inclusive agreement has not been reached regarding the best anthropometric indices to assess the risk of MetS in PCOS patients.

Kahn described lipid accumulation product (LAP) as a better indicator than BMI for identifying the risk of CVD for the first time\cite{28} in the National Health and Nutrition Examination Survey III. LAP is based on the combination of waist measurements and fasting triglycerides levels, considering both the anatomical and physiological changes related to lipid over-accumulation. Several studies have shown that LAP was closely associated with MetS in different diagnostic criteria [Table 1]. Therefore, LAP might be an easy and powerful marker for predicting the risk of MetS.

Early diagnosis of MetS in PCOS patients potentially will prevent further complications of metabolic disturbances such as CVD. MetS diagnosis is based on the combination of anthropometric and laboratory biochemical evaluations. Therefore, there is a necessity for using the simple, cost-effective, precise, and comprehensive indices of MetS risk assessment in PCOS women during the extended period of transition from subclinical to obvious CVD.

This paper analysed the accuracy and association of different anthropometric indices and LAP in PCOS women with MetS in certain geographic area.

**METHODS**

This cross-sectional study was carried out in women with PCOS based on observation and samples collected from PCOS patients (150) and healthy women, i.e. control (100) in December 2017 to October 2019, from private hospitals of Mysuru, Karnataka, India, namely Ashwini hospital, Santasa IVF Centre, and Mediwave Infertility hospital. According to previous studies,\cite{29,30} we assumed that the prevalence of PCOS in south of India is around 9.13%. The following formula was utilised to calculate the suitable sample size in a prevalence study.\cite{31} Based on the formula, in this study the minimum sample size with a 95% confidence level should be 128 individuals, but we increased the sample size to 150 in order to achieve more precise results.

\[ n = \frac{Z^2P (1 − P)}{d^2} \]

\( n \): Sample size

\( Z \): Statistic corresponding to the level of confidence

\( P \): Expected prevalence

\( d \): Precision (corresponding to impact size).

In this study, the following inclusion criteria were used: PCOS women aged 18–45 as reproductive age diagnosed by Rotterdam criteria\cite{32} that require the presence of at least two criteria out of the following three:

- Oligo- and/or anovulation – whether oligoamenorrhea or amenorrhea was present.
- Clinical and/or biochemical signs of hyperandrogenemia.
- Polycystic ovaries on ultrasound.

Women with a medical history of Cushing’s syndrome, adrenal 21-hydroxylase deficiency, androgen-secreting tumors, thyroid dysfunction, hyperprolactinemia were excluded from the study. Women without any signs of the above criteria were used as a control for the studies.

General information for each patient, such as name, age, personal medical history, and information related to diagnosis and treatment of PCOS, was collected. Systolic and diastolic blood pressures (SBP and DBP) were measured with the subjects in the sitting position on the right hand. Weight, height, hip, and waist were measured precisely. All measurements were performed in a standing position with feet together, relaxed abdomen, and arms at their sides. The WC of subjects was measured by placing a soft tape measure at the midpoint between the lowest rib and iliac crest, and hip circumference (HC) was measured at the widest level of the great trochanters. 2-ml blood samples were drawn from all the subjects after a 12-h overnight fast. Plasma
Table 1: Studies on association of anthropometric indices/lipid accumulation product with metabolic syndrome in different population

| Region          | Population                                      | Subjects (n) | Age (years) | Anthropometric indices and LAP | MetS: Population type (diagnostic criteria) | ROC curve analysis index (gender):AUC | Cut-off |
|-----------------|-------------------------------------------------|--------------|-------------|-------------------------------|---------------------------------------------|--------------------------------------|---------|
| Asia            | Japanese population[12]                         | 629          | 51-75       | BMI, WC, WHR, WHtR, LAP       | MetS-general (IDF)                          | WC (male): 0.65                      | WC (male): 85 |
|                 | Male: 315                                       |              |             |                               |                                             | WC (female): 0.72                    | WC (female): 90 |
|                 | Female: 314                                     |              |             |                               |                                             |                                      |         |
|                 | Chinese population[13]                          | 2947         | >20         | BMI, WC, WHR, WHtR            | MetS-general (CDS IDF, NHLBI/AHA)           | WLH: 0.72                           | WLH: 2.5  |
|                 | Male: 1674                                      |              |             |                               |                                             |                                      |         |
|                 | Female: 1273                                    |              |             |                               |                                             |                                      |         |
|                 | Jordanian population[14]                        | 500          | 20-85       | BMI, WC, WHR, WHtR            | MetS-general population (IDF)               | WLH: 0.72                           | WLH: 2.5  |
|                 | Male: 212                                       |              |             |                               |                                             |                                      |         |
|                 | Female: 288                                     |              |             |                               |                                             |                                      |         |
|                 | Taiwanese adults[15]                            | 513          | ≥50         | BMI, WC, WHR, WHtR, LAP       | MetS-general (MS-TW)                        | LAP: 0.90                           | LAP: 25.9 |
|                 | Male: 266                                       |              |             |                               |                                             |                                      |         |
|                 | Female: 247                                     |              |             |                               |                                             |                                      |         |
|                 | Iranian population[16]                          | 206          | >19         | BMI, WC, WHR, WHtR            | MetS-eldery population (NCEP ATP III)       | WC: 0.68                            | WC: 94.5 |
|                 | Male: 167                                       |              |             |                               |                                             |                                      |         |
|                 | Female: 328                                     |              |             |                               |                                             |                                      |         |
|                 | Jordanian population[17]                        | 630          | 20-70       | BMI, WC, WHR, WHtR            | MetS-general population (IDF)               | WC (male): 0.85                      | WC (male): 98.5 |
|                 | Male: 308                                       |              |             |                               |                                             |                                      |         |
|                 | Female: 322                                     |              |             |                               |                                             |                                      |         |
|                 | Chinese population[18]                          | 1029         | 47±13.6     | BMI, WC, VAI, LAP, BAI, WHtR  | MetS-Low income rural adults (JIS)           | VAI: 0.94                           | VAI: 28  |
|                 | Thai women[19]                                  | 441          | 25.4±5.6    | BMI, WC, WHR, WHtR, VAI       | MetS-PCOS (IDF)                             | VAI: 0.94                           | VAI: 28  |
|                 | Patient: 399                                    |              |             |                               |                                             |                                      |         |
|                 | Control: 42                                     |              |             |                               |                                             |                                      |         |
|                 | Chinese adults[20]                              | 379          | 40-65       | BMI, WC, WHR, ABSI, AVI, BAI, BRI, CI, VAI | MetS-general (IDF) | BMI (male): 0.77 | BMI (male): 24.94 |
|                 | Male: 198                                       |              |             |                               |                                             |                                      |         |
|                 | Female: 181                                     |              |             |                               |                                             |                                      |         |
|                 | Iranian population[21]                          | 5312         | 18-74       | BMI, WC, WHR, WHtR, VAI       | MetS-general (NCEP ATP III, AHA/NHLBI, IDF, JIS) | VAI (male): 0.82-0.87* | VAI (male): 1.92-2.5* |
|                 | Male: 2972                                      |              |             |                               |                                             |                                      |         |
|                 | Female: 2340                                    |              |             |                               |                                             |                                      |         |
|                 | European sicilian population[22]                | 1764         | 20-40       | BMI, WC, VAI                  | MetS-Primary care Patients (NCEP-ATPIII)    | VAI: 0.78-0.99*                      | VAI: 1.92-2.5* |
|                 | Caucasian serbian women[23]                     | 267          | 25±4.89     | BMI, WC, LAP                  | MetS-PCOS (NCEP ATP III, IDF and JIS)       | LAP: 0.97                           | LAP: 25.9 |
|                 | Patient: 222                                    |              |             |                               |                                             |                                      |         |
|                 | Control: 45                                     |              |             |                               |                                             |                                      |         |
|                 | Polish women[24]                                | 12328        | 37-66       | BMI, WC, WHR, WHtR, VAI       | MetS-general (IDF)                          | WHR (male): 0.76                      | WHR (male): 0.56 |
|                 | Male: 4094                                      |              |             |                               |                                             |                                      |         |
|                 | Female: 8234                                    |              |             |                               |                                             |                                      |         |
|                 | Polish population[25]                           | 113          | 27.2±4.5    | WC, WHR, WHtR, CI             | MetS-PCOS (NCEP ATP-III)                    | WC: 0.83                           | WC: 95  |
|                 | Brazilian women[26]                             |              |             |                               |                                             |                                      |         |
|                 | Patient: 113                                    |              |             |                               |                                             |                                      |         |

Contd...
glucose was measured by glucose oxidase-peroxidase assay (ARKRAY kit, Mumbai, Maharashtra, India). Lipid profile including cholesterol, triglycerides, and high-density lipoprotein (HDL) were estimated by enzymatic assay (Meril kit, Vapi, Gujarat, India), and low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) were calculated by Friedewald equation.[33,34] Fasting insulin level was determined by ELISA (Prime Biomed, Bangaluru, Karnataka, India).

We applied the International Diabetes Federation criteria (IDF) and South Asian-specific abdominal obesity standards for the diagnosis of MetS in all subjects in this study.[35] Conforming to the new definition, a person assessed as having MetS must have central obesity (in this study, South Asian female WC ≥80 cm), plus any two of the following four factors: (i) elevated triglycerides (triglycerides ≥150 mg/dL); (ii) reduced HDL (HDL <50 mg/dL in female); (iii) raised blood pressure (SBP ≥130 mmHg, DBP ≥85 mmHg); (iv) and high fasting plasma glucose (FPG ≥100 mg/dL).

LAP was measured as follows:[28]

Female LAP = [waist (cm) – 58] × triglycerides concentration (mmol/l)
BMI, WHR, WHtR, CI, AVI, ABSI, BAI, and VAI were calculated: [27,36,37]

BMI = Weight (kg)/Height² (m)
CI = WC (m)/0.109√[weight (kg)/height (m)]
AVI= [2 WC² (cm) +0.7 (WC – HC)² (cm)]/1000
ABSI = WC (cm)/(BMI²/3 Hight¹/2)
BAI = HC (cm)/Height (m)¹.5 – 18
VAI (Female) = [WC (cm)/36.58+ (1.89 × BMI)] × triglycerides (mmol/l)/0.81 × 1.52/HDG (mmol/l)

The study was approved by the Institutional Human Ethical Committee, University of Mysore, Manasagangotri, Mysore (No. 151/PhD/2017-18), in accordance with the Helsinki Declaration (as revised in 2013), and written consent was obtained from all the subjects.

Statistical analysis was employed using the Statistical Package for the Social Sciences software SPSS, version 23.0; IBM (IBM Corp. Armonk, NY, USA). Results were expressed as mean ± standard deviation. The normality of data distribution of continuous variables was subjected to the Shapiro–Wilks test. Student’s t-test and univariate analysis of variance were applied for analysing the differences between groups. Homogeneity of variance was tested using the Leven’s test, and to identify any heterogeneity of variance, Games–Howell test was performed. For multiple comparisons, post hoc test was executed. A P < 0.05 was reflected as statistically significant.

Multiple binary logistic regression was applied to analyse the determinants of MetS. Receiver operating characteristic (ROC) curves were created for each continuous variable, which showed a significant association with MetS. The area under curves was calculated to identify the accuracy of determinants of MetS and LAP and anthropometric indices. Optimal new cutoff points were determined by Youden’s Index (sensitivity + specificity – 1). The ability of each variable to predict MetS was shown by the area under the curve with the standard error of the mean and 95% confidence intervals (95% CIs). For determinant variables of MetS, their IDF criteria known cutoff values were used to compare their sensitivity and specificity and the sensitivity and specificity of the new cutoff values determined by Yoden’s Index in our study population.

**RESULTS**

Comparing the clinical and anthropometric characteristics between PCOS and control eligible candidates, 150 patients and 100 controls were compared in the present study. The PCOS and control samples’ mean age

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### Table 1: Contd...

| Region | Population | Subjects (n) | Age (years) | Anthropometric indices and LAP | MetS; Population type (diagnostic criteria) | ROC curve analysis index (gender):AUC | Cut-off |
|--------|------------|--------------|-------------|--------------------------------|---------------------------------------------|--------------------------------------|---------|
| Argentinian women[26] | 198 | Patient: 110, Control: 88 | 18-35 | BMI, WC, VAI, LAP | MetS-PCOS | Nil | VAI: 2.19, LAP: 18.24 |

*AUC range for significant parameters according to different diagnostic criteria as mentioned in the study, 'AUC and cutoff range for significant parameters according to age quintile as mentioned in the study. Values are expressed as mean±SD, bold parameters are statistically significant. AUC=Area under the curve, MetS=Metabolic syndrome, IDF=International Diabetes Federation, CDS=Chinese Diabetes Society, NHLBI/AHA=National Heart, Lung, and Blood Institute and the American Heart Association, MS-TW=MS using Taiwanese criteria, NCEP ATP III=The National Cholesterol Education Program Adult Treatment Panel III, JIS=Joint Interim Statement, BMI=Body mass index, WC=Waist circumference, WHR=Waist-to-hip ratio, WHtR=Waist-to-height ratio, CI=Conisity index, AVI=Abdominal volume index, BAI=Body adiposity index, ABSI=A body shape index, VAI=Visceral adiposity index, LAP=Lipid accumulation product, PCOS=Polycystic ovary syndrome, CUN-BAE=Clínica universidad de Navarra-Body adiposity estimator, BRI=Body roundness index.
was 25.78 ± 5.00 and 24.79 ± 4.66 years, respectively. Anthropometric parameters such as WC and WHtR determining central obesity were found significantly increased in PCOS group in comparison to control group. LAP in the PCOS and control were 63.49 ± 48.96 and 43.74 ± 20.85, respectively, that shows a significant difference in PCOS group in comparison to control group. Metabolic and anthropometric characteristics are expressed in Table 2, according to which there was a significant difference in DBP, FPG, fasting insulin, BMI, WC, WHR, WHtR, CI, AVI, BAI, VAI, cholesterol, triglycerides, HDL, LDL, and LAP between PCOS and control group.

The women with PCOS were subgrouped into MetS and non-MetS according to IDF criteria. The prevalence of the MetS, according to the IDF for the PCOS women, was 59.3% (n = 89). The clinical and anthropometric characteristics of three groups (PCOS with and without MetS and control) are presented in Table 3. Multiple comparisons between PCOS with MetS and without MetS and control were performed. Compared to both control and PCOS without MetS, participants with MetS had a significantly higher level of SBP, DBP, FPG, fasting insulin, lipid profile (cholesterol, triglycerides, LDL, and VLDL), and LAP but the lower level of HDL. Moreover, the anthropometric indices, including BMI, WC, WHR, WHtR, CI, AVI, BAI, and especially VAI, were significantly elevated in the cases of PCOS with MetS. ABSI was increased in PCOS with MetS but not significantly.

Multiple binary logistic regression showed that LAP, VAI, DBP, and fasting glucose were significantly associated with MetS. We applied all of the variables in multiple binary logistic regression analysis model. In step 1, DBP was entered in step 2, VAI, then FPG, and in the last stage, LAP. In the final model, VAI, DBP, FPG, and LAP remained significantly associated with MetS defined by IDF [Table 4]. VAI was a more useful indicator than others. The second indicator was DBP, but the model was more robust when all parameters were present.

We analysed the diagnostic test accuracy of the MetS determinants and significantly associated anthropometric parameters with MetS [Table 3] by ROC curve analysis. The following cutoff values were identified for: VAI 6.05, DBP 81.4 mmHg, triglycerides 152.4 mg/dL, LAP 53, FPG 99.75 mg/dL, WC 88.5 cm, WHR 0.92, SBP 123.15 mmHg, WHtR 55.85, CI 1.34, BMI 23.2 kg/m2, AVI 19.48, insulin 11.53 mU/L, BAI 40.25, and HDL 37.90 mg/dL [Table 5].

As presented in Table 5, VAI, DBP, triglycerides, and LAP showed the highest MetS diagnostic accuracy. Other parameters’ accuracy for the MetS are presented in Table 5. AVI cutoff value 6.05 showed sensitivity: 0.85 and specificity: 0.85 with higher positive predictive value (0.89) than negative predictive value (0.79) for MetS.

ROC curves for determinants of MetS according to the final model of logistic regression are plotted in Figure 1.

### Discussion

Our study proposes VAI and LAP as simple and cost-effective indices for assessing the risk of MetS in women with PCOS in certain geographic area. Our study identified that VAI provided the highest diagnostic accuracy among known and associated determinants for MetS. MetS has a variable frequency of up to 50% among PCOS women, which varies between populations and ethnicities.\[2,38-40\] The prevalence of MetS within our population of PCOS women was 59.3%, with a mean age of 25.78 ± 5.00 years. This was higher than the prevalence of 47.4% identified previously using

**Table 2: Clinical and anthropometric characteristics in polycystic ovary syndrome in control groups**

| Analyses                  | PCOS (n=150) | Control (n=100) | P  |
|---------------------------|--------------|-----------------|----|
| Age (year)                | 25.78±5.00   | 24.79±4.66      | 0.114 |
| SBP (mmHg)                | 125.26±10.00 | 123.88±8.56     | 0.246 |
| DBP (mmHg)                | 80.55±5.29   | 78.79±5.36      | 0.011* |
| FPG (mg/dL)              | 94.89±15.26  | 90.70±12.58     | 0.004* |
| Fasting insulin (mU/L)  | 15.50±5.78   | 11.84±4.79      | <0.001* |
| BMI (kg/m²)              | 26.73±5.28   | 23.07±3.71      | <0.001* |
| WC (cm)                  | 92.2±12.6    | 85.35±9.9       | <0.001* |
| WHR                      | 0.91±0.08    | 0.89±0.04       | 0.017* |
| WHtR                     | 61.33±9.89   | 54.18±5.79      | <0.001* |
| CI                       | 1.32±0.12    | 1.29±0.09       | 0.068 |
| AVI                      | 17.72±4.46   | 14.8±3.24       | <0.001* |
| BAI                      | 33.98±6.64   | 29.21±4.52      | <0.001* |
| ABSI                     | 0.09±0.01    | 0.08±0.006      | 0.082 |
| VAI                      | 9.17±8.08    | 6.61±2.25       | <0.001* |
| Cholesterol (mg/dL)      | 212.83±51.12 | 184.84±61.76    | <0.001* |
| Triglycerides (mg/dL)    | 154.08±76.74 | 140.19±32.43    | 0.05*  |
| HDL (mg/dL)              | 39.42±13.56  | 44.36±9.30      | 0.001* |
| LDL (mg/dL)              | 142.58±44.67 | 115.74±59.22    | <0.001* |
| VLDL (mg/dL)             | 30.81±15.34  | 28.56±5.95      | 0.106 |
| LAP                      | 63.49±48.96  | 43.74±20.85     | <0.001* |

Values are expressed as mean±SD, *P<0.05 was considered as significant. SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, BMI=Body mass index, WC=Waist circumference, WHR=waist-to-hip ratio, WHtR=waist-to-height ratio, CI=Conicity index, AVI=Abdominal volume index, BAI=Body adiposity index, ABSI=A body shape index, VAI=Visceral adiposity index, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, VLDL=Very low-density lipoprotein, LAP=Lipid accumulation product, PCOS=Polycystic ovary syndrome
IDF criteria by Bhattacharya,\(^{(41)}\) as well as the 53.3% and 37.5% prevalence identified on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria\(^{(42)}\) and modified NCEP ATP III,\(^{(43)}\) respectively, in various Indian studies. This study re-establishes a relationship between obesity and the MetS. The prevalence of obesity is increasing worldwide, and the high prevalence rate of MetS in our study reiterates that obesity is a direct contributing factor of MetS in this population. For the first time, our results established a strong association between VAI with MetS in a selected south Indian population of women with PCOS. The final model obtained from logistic regression shows the strong association of VAI, followed by DBP, FPG, and LAP with MetS, where DBP and FPG were previously defined as determinants of MetS by IDF criteria.

WC as a primary clinical parameter for estimating increased visceral fat does not help differentiate between subcutaneous and visceral fat, especially additional fat, and subsequent dysfunctions associated with

| Table 3: Clinical and anthropometric characteristics of polycystic ovary syndrome with and without metabolic syndrome according to International Diabetes Federation criteria |
|---------------------------------------------------------------|
| **Analyses** | **PCOS with MetS (n=89)** | **PCOS without MetS (n=61)** | **Control (n=100)** | **P** |
| Age (year) | 26.35±5.30* | 24.97±4.46* | 24.79±4.66* | 0.067 |
| SBP (mmHg) | 128.98±9.60* | 119.85±7.95* | 123.89±8.57* | <0.001* |
| DBP (mmHg) | 83.11±6.33c | 76.84±3.62c | 78.79±5.36c | <0.001* |
| Fasting insulin (mU/L) | 99.89±15.42c | 87.62±11.80c | 90.71±12.58c | <0.001* |
| BMI (kg/m\(^2\)) | 28.05±5.22c | 24.81±4.80c | 23.07±3.72c | <0.001* |
| WC (cm) | 95.84±12.51c | 86.91±10.83c | 85.35±9.41c | <0.001* |
| WHR | 13.5±0.14c | 12.9±0.10c | 13.0±0.09c | 0.004* |
| AVI | 18.67±4.74c | 16.35±3.63c | 14.81±3.24c | <0.001* |
| BAI | 34.57±6.76c | 33.12±6.43c | 29.22±4.52c | <0.001* |
| ABSI | 0.10±0.12c | 0.09±0.08c | 0.08±0.01c | 0.306 |
| VAI | 12.00±9.47a | 5.04±1.23b | 6.61±2.25a | <0.001* |
| Cholesterol (mg/dL) | 224.47±53.84a | 195.86±41.79a | 184.85±61.76a | <0.001* |
| Triglycerides (mg/dL) | 182.62±86.05b | 112.44±28.18a | 140.19±32.44a | <0.001* |
| HDL (mg/dL) | 35.38±12.14c | 45.34±45.34c | 44.36±9.31c | <0.001* |
| LDL (mg/dL) | 152.56±47.59b | 128.03±35.68a | 115.74±59.23a | <0.001* |
| VLDL (mg/dL) | 36.52±17.21b | 22.49±5.64c | 28.56±5.95c | <0.001* |
| LAP | 81.51±55.14b | 37.20±17.65a | 43.74±20.86a | <0.001* |

Values are expressed as mean±SD. Different letters “a,b,c” express statistical differences between groups in univariate analysis. *P≤0.05 was considered as significant. SBP=Systolic blood pressure, DBP=Diastolic blood pressure, FPG=Fasting plasma glucose, BMI=Body mass index, WC=Waist circumference, WHR=Waist-to-hip ratio, WHtR=Waist-to-height ratio, CI=Conisity index, AVI=Abdominal volume index, BAI=Body adiposity index, ABSI=A body shape index, VAI=Visceral adiposity index, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, VLDL=Very low-density lipoprotein, LAP=Lipid accumulation product, PCOS=Polycystic ovary syndrome, SD=Standard deviation

| Table 4: Determinants of metabolic syndrome using International Diabetes Federation criteria |
|------------------------|-----------------|-------------|--------|
| Variable | RR | 95% CI | P |
| VAI | 4.03 | 1.86-8.73 | 0.001 |
| DBS | 1.87 | 1.37-2.56 | 0.001 |
| FPG | 1.13 | 1.04-1.23 | 0.002 |
| LAP | 1.05 | 1.00-1.10 | 0.027 |

Evaluated by multiple binary logistic regression. RR=Relative risk, CI=Confidence interval, VAI=Visceral adiposity index, FPG=Fasting plasma glucose, LAP=Lipid accumulation product, DBS=Diastolic blood pressure

IDF criteria by Bhattacharya,\(^{(41)}\) as well as the 53.3% and 37.5% prevalence identified on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria\(^{(42)}\) and modified NCEP ATP III,\(^{(43)}\) respectively, in various Indian studies. This study re-establishes a relationship between obesity and the MetS. The prevalence of obesity is increasing worldwide, and the high prevalence rate of MetS in our study reiterates that obesity is a direct contributing factor of MetS in this population. For the first time, our results established a strong association between VAI with MetS in a selected south Indian population of women with PCOS. The final model obtained from logistic regression shows the strong association of VAI, followed by DBP, FPG, and LAP with MetS, where DBP and FPG were previously defined as determinants of MetS by IDF criteria.

WC as a primary clinical parameter for estimating increased visceral fat does not help differentiate between subcutaneous and visceral fat, especially additional fat, and subsequent dysfunctions associated with
Table 5: Area under the ROC Curve for identification of accuracy and cutoff value for determinant of metabolic syndrome

| Variable | AUC      | P       | 95% CI   | Cut-off | SEN (%) | SP (%) |
|----------|----------|---------|----------|---------|---------|--------|
| VAI      | 0.91±0.02| <0.001  | 0.86-0.95| 6.05    | 0.85    | 0.85   |
| DBP      | 0.85±0.03| <0.001  | 0.79-0.91| 81.4    | 0.66    | 0.95   |
| Triglycerides | 0.81±0.03| <0.001  | 0.74-0.88| 152.4   | 0.51    | 0.96   |
| LAP      | 0.81±0.03| <0.001  | 0.74-0.87| 53      | 0.68    | 0.80   |
| FPG      | 0.77±0.03| <0.001  | 0.70-0.85| 99.75   | 0.62    | 0.93   |
| WHR      | 0.77±0.04| <0.001  | 0.69-0.85| 0.92    | 0.64    | 0.78   |
| SBP      | 0.76±0.03| <0.001  | 0.68-0.83| 123.15  | 0.71    | 0.80   |
| WC       | 0.70±0.04| <0.001  | 0.61-0.78| 88.5    | 0.71    | 0.60   |
| WHtR     | 0.65±0.04| 0.001   | 0.56-0.74| 55.85   | 0.83    | 0.44   |
| CI       | 0.64±0.04| 0.003   | 0.55-0.73| 1.34    | 0.56    | 0.70   |
| BMI      | 0.64±0.04| 0.003   | 0.55-0.73| 23.2    | 0.93    | 0.41   |
| AVI      | 0.64±0.04| 0.004   | 0.55-0.72| 19.48   | 0.39    | 0.85   |
| Insulin  | 0.57±0.04| 0.137   | 0.47-0.66| 11.53   | 0.84    | 0.34   |
| BAI      | 0.54±0.04| 0.326   | 0.45-0.64| 40.25   | 0.24    | 0.90   |
| HDL      | 0.27±0.04| 0.001   | 0.19-0.35| 37.90   | 0.31    | 0.34   |

ROC= Receiver operating characteristic curve, AUC=Area under the curve, SEN=Sensitivity, SP=Specificity, VAI=Visceral adiposity index, DBP=Diastolic blood pressures, FPG=Fasting plasma glucose, LAP=Lipid accumulation product, WHR=Waist-to-hip ratio, WHtR=Waist-to-height ratio, CI=Conisity index, SBP=Systolic blood pressure, WC=Waist circumference, AVI=Abdominal volume index, BMI=Body mass index, BAI=Body adiposity index, HDL=High-density lipoprotein, CI=Confidence interval

different structures of the body.[44] A study by Amato et al. in 2010 proposed VAI as a substitute marker of “adipose tissue dysfunction.” VAI showed a significant association with all MetS factors and cardiovascular events, which may be justified since VAI assessment includes physical and metabolic parameters. On the other hand, possibly, VAI indirectly indicates other risk factors, such as increased lipolysis, modified production of adipocytokines, and plasma free fatty acids, which are not indicated by BMI, WC, triglycerides, and HDL parameters independently. Consequently, VAI might be a superior index of fat distribution and function.[45] As represented in Table 1, several studies have shown that VAI has a strong association with MetS risk factors and suggested it as a good predictor for MetS.[18-20] In another study, VAI, WC, and WHtR were proposed as the best predictors for individual MetS components in a Peruvian population.[46] Our findings established a new VAI cut point >6.05, which is higher than previously reported cut point values in other populations investigated.[19,21-23,26] This observation can be explained by the fact that south Indian PCOS patients in this study have shown more central obesity than BMI, and the mean baseline of WC and triglycerides was remarkably elevated with significantly reduced HDL in the MetS group.

The second highest test accuracy was DBP, a recognized clinical marker for diagnosing MetS in the general population.[35,47] Raised blood pressure associates with obesity and glucose intolerance and frequently occurs in insulin-resistant persons. The association’s impact differs significantly from one population to another.[47] Our findings show the strong effect of DBP in MetS. It might be due to DBP being a more potent cardiovascular risk factor than SBP until the age of 50.[48] In this study, the mean age of patients was 25.78 ± 5.00 years.

FPG shows a significant association with MetS in agreement with several earlier studies conducted globally.[49,50] An elevated level of blood glucose is a severe risk factor for a person diagnosed with diabetes and hyperglycemia. It might be due to the increasing triglycerides and decreasing HDL that increase CVD risk.[47]

Another significant predictive marker identified in this study was previously proposed by Henry Kahn, in 2005, based on the measurement of WC. Lipid overaccumulation, associated with metabolic and cardiovascular risk factors, can be assessed through LAP in adults.[28] One study confirmed the diagnostic accuracy of LAP in predicting metabolic disturbances associated with insulin resistance among young Argentinian PCOS patients.[50] Furthermore, this index was associated with the homeostatic model assessment in 51 Brazilian PCOS patients[51] and impaired glucose tolerance in Caucasian women.[52] Macut et al. in 2016 have shown that LAP is an independent and straightforward indicator for the assessment of MetS among PCOS women of Caucasian origin.[22] One study on the Chinese population has demonstrated the relation between LAP and MetS in PCOS as well.[53]

Furthermore, this index was associated with the homeostatic model assessment in 51 Brazilian PCOS patients[51] and impaired glucose tolerance in Caucasian women.[52] Macut et al. in 2016 have shown that LAP is an independent and straightforward indicator for the assessment of MetS among PCOS women of Caucasian origin.[22] One study on the Chinese population has demonstrated the relation between LAP and MetS in PCOS as well.[53]
Our analysis showed that the LAP optimal cutoff value for determining MetS was >53. We support the proposal that each population should establish its own cutoff values.[28] Our data showed that LAP and triglycerides shared the same level of accuracy. However, in the final model of logistic regression, LAP displayed a significant association with MetS in south Indian women with PCOS. It might be justified by the fact that LAP, including the combination of triglycerides and WC, increases the chance of MetS than triglycerides independently.

Some limitations in the current study should be contemplated. This study was limited to the PCOS women from certain geographic area and indicates two new indexes VAI and LAP, as statistically significant determinants of MetS in women with PCOS. Similar studies need to be carried out in other populations to infer if these new indexes exhibit population specificity. IDF criteria were used in the current study to define MetS. Therefore, further studies are required to determine whether the results are applicable under other well-known criteria.

**Conclusions**

The present study suggests two new indexes VAI and LAP, as statistically significant determinants of MetS in south Indian women with PCOS, in addition to the prevalently used predictors DBP and FPG. The high diagnostic accuracy of VAI indicates the strength of the combination of WC, BMI, serum triglycerides, and HDL as a simple index instead of utilising them independently for determining the MetS and in the subsequent prediction of CVD in PCOS women.

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**Conflicts of interest**

There are no conflicts of interest.

**Data availability statement**

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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