Research Article

COMPARISON OF LIPID ACCUMULATION PRODUCT INDEX: A CHEAP MARKER OF CARDIOVASCULAR RISK WITH BODY MASS INDEX, BODY ADIPOSITY INDEX AND WAIST HIP RATIO IN NEWLY DIAGNOSED POLYCYSTIC OVARY SYNDROME

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ARTICLE INFO

ABSTRACT

Background: Metabolic derangements of polycystic ovary syndrome (PCOS) are contributing factors of increased the risk of cardiovascular disease. Lipid accumulation product (LAP) index as a cheap and reliable marker of cardiovascular risk and insulin resistance (IR) and metabolic syndrome (MS).

Objective: The aim of this study was to estimate LAP index and compare with BMI, body adiposity index (BAI) and waist hip ratio (W/H ratio) in newly diagnosed PCOS patients with controls.

Materials and Methods: This is a case-control study including 30 PCOS patients aged between 15 and 40 years and 30 age matched healthy controls. Fasting sample were obtained for lipid profile analysis after getting written consent. Anthropometric measurements were taken as per protocol. LAP index, BMI, BAI and W/H ratio were calculated and analysed statistically.

Results: Among PCOS patients, LAP score had significantly positive correlation with patient's age (r = 0.42 & P=0.02), BMI (r = 0.441 & P=0.015), BAI (r = 0.45 & P=0.013) and W/H ratio (r = 0.405 & P=0.026). Among controls, LAP score had more significant positive correlation with W/H ratio (r = 0.546 & P=0.002). LAP score and W/H ratio had highly significant P value (P= 0.000) and BMI showed P= 0.003 while comparing PCOS patients and controls.

Conclusion: LAP index, an easily obtainable, reliable, cheap marker of cardiovascular risk, IR and MS. The early deduction and intervention could be possible to prevent metabolic and clinical complications among PCOS patients by LAP scoring.

INTRODUCTION

Polycystic ovary syndrome (PCOS), is the most prevalent endocrinopathy in women of reproductive age which is a metabolic disorder with ovulatory dysfunction, hyperandrogenism and insulin resistance (IR) which are contributing factors for metabolic syndrome (MS). Insulin resistance, an independent risk factor for cardiovascular disease, is a common feature in these patients.[1]

The lipid accumulation product (LAP) index (describing lipid over accumulation) which combines waist circumference (WC) & triglyceride concentration for identifying adults with insulin resistance, elevated glucose, and diabetes.[2]

Compared to BMI, LAP might better predict the incidence of cardiovascular disease, but this hypothesis needs prospective testing.[3] LAP has been advocated as a simple clinical indicator of MS.[4]

Body adiposity index (BAI) was used to measure the %fat and was better than BMI as an indicator of adiposity[5]. The aim of this study was to estimate LAP index as a cheap marker of cardiovascular risk in newly diagnosed PCOS patients.

MATERIALS AND METHODS

This was a case control study carried out with women consulting at the Out Patient Department of Obstetrics and Gynaecology at Pt. B. D. Sharma PGIMS, Rohtak were included in this study after obtaining written consent.

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Inclusion criteria

Newly diagnosed PCOS patients (according to Rotterdam criteria) and healthy controls, not on any treatment, fasting of 8-12 hours, of aged 15 to 40 years.

Exclusion criteria

Pregnancy, non pregnant Women with BMI more than 40 kg/m^2 or type2 diabetes were excluded.

Measurements

Anthropometric measurements were body weight, height and WC (waist measured at the midpoint between the lower rib margin and the iliac crest in a plane that is perpendicular to the long axis of the body, with the subject standing balanced on both feet, approximately 20 cm apart, with both arms hanging freely) (World Health Organization, 1995; Donato *et al.*, 2006; Toscani *et al.*, 2007). Hip circumference (HC) was taken at the widest portion of buttocks.

Assays

Serum triglycerides was performed by enzymatic method on the RANDOX (Randox Laboratories Limited, UK), according to the manufacturer's specifications by using proprietary reagents at the Department of Biochemistry. Intra-assay analytical CV's was determined by two levels of control materials (Randox Laboratories Limited, UK) (N = 10, from each level on the same plate) on the same day before biochemical analysis. The details of methods of each test were mentioned in the table I & II.

Table I

S.No.	Investigation	Method	Reference value
1.	Fasting blood glucose	Enzymatic (GOD – POD)	75 - 115 mg/L
2.	Triglycerides	Enzymatic	60 - 160 mg/L
3.	Total cholesterol	Enzymatic	130 - 230 mg/L
4.	HDL-cholesterol	Enzymatic	30 - 60 mg/L
5.	LDL- cholesterol	Enzymatic	≤ 160 mg/L
6.	HbA$_{1C}$	latex agglutination immuno inhibition	<5.7%

VLDL value was calculated by Friedwald equation = [Triglycerides/5] mg/L.

Table II

S.No.	Investigation	Method	Reference value
1.	Free Testosterone	Enzyme Linked Immuno Sorbent Assay (ELISA)	0.01-7.01 pg/mL
2.	DHEAS	ELISA	0.46 – 2.75 µg/mL
3.	Estrone	ELISA	25-350 pg/mL.
4.	Total testosterone	Chemiluminescence	14-76 ng/dL
5.	Prolactin	Chemiluminescence	2.8-28.2 ng/mL
6.	LH	Chemiluminescence	1.9-12.5 mIU/mL
7.	FSH	Chemiluminescence	2.5-10.2 mIU/mL
8.	TSH	Immuno radiometric assay	0.3-5.0 µU/mL
9.	Hemoglobin	Sahli's method	12-14 g/dL

Calculations

Formulae used in this study were:

LAP (women) = [waist circumference (cm)-58] × [triglycerides (mmol/L)].

BMI = [present weight(kg) / height(m)^2]

BAI = [hip circumference (cm) / height(m)$^{1.5}$] - 18

W/H ratio = waist circumference / hip circumference

Statistical Analysis

The correlation between variables was tested using the two-tailed Pearson correlation test. Unpaired 't' test applied to compare variables between PCOS cases and controls. Data were considered to be significant at P < 0.05. All analyses were performed by using the Statistical Package (IBM SPSS).

RESULTS

From this study, we found that BMI (cut off 25), 53.3% of PCOS patients and 23.3% of controls were overweight. With respect to BAI (cut off 33%), we observed that 3.3% were obese and 40% were overweight among PCOS and 23.3% were overweight among controls.

93.3% of PCOS and 6.7% of controls showed higher LAP score (cut off 34.5). 50% of PCOS and 13.3% of controls had higher W/H ratio (cut off 0.8). 23 PCOS patients and 4 controls had increased serum triglycerides level.

Chart-1: Comparison of Percentage of Lap, Bmi, W/H & TG among Cases and Controls

Among PCOS patients, LAP score had significant positive correlation with patient's age (r = 0.42 & p=0.02), BMI (r = 0.441 & p=0.015), BAI (r = 0.45 & p=0.013) and W/H ratio (r = 0.405 & p=0.026). W/H ratio had positive correlation only with LAP score but not with other parameters.

Among controls, LAP score had more significant positive correlation with W/H ratio only (r = 0.546 & p=0.002) but not with other parameters.

We observed that BMI had highly significant positive correlation with BAI having r = 0.826 & p=0.000 among PCOS and r = 0.483 & p=0.007 among controls.

By applying unpaired 't' test, we found that LAP score and W/H ratio had highly significant p value (p= 0.000) and BMI showed p= 0.003 while comparing PCOS patients and controls. BAI & W/H ratio were of significant positive correlation with age (p=0.000) in both cases & controls but BMI had positive correlation with age in cases only (p=0.005) & not with control (p=0.253).

Table III

PARAMETERS	CASE(Mean)	CONTROL(Mean)
LAP	131.64	13.75
BMI	26.09	23.19
BAI	31.9	30.7
W/H Ratio	0.8	0.7

Table IV Clinical data mean of PCOS cases and controls and their significance

S.No.	PARAMETERS	MEAN CASES (n = 30)	MEAN CONTROLS (n = 30)	't' value	p value
1.	Age	23.26±5.65	23.6±6.45	-0.213	0.832
2.	BMI	26.09±4.2	22.9±3.3	3.245	**0.002***
3.	WC	78.08±9.8	70.06±8.5	3.360	**0.001****
4.	HC	97.41±9.4	92±7.8	2.416	**0.019***
5.	WC / HC	0.799±0.56	0.762±0.9	1.940	0.057
6.	SBP	116.7±12.57	109.9±6.89	2.598	0.12
7.	DBP	79±7.4	71±6.2	4.083	**0.000****
8.	Hirsutism score	7.6±3.9	2.67±1.52	6.444	**0.000****

BMI - Body mass index is calculated by formula[weight(kg) / height(m)^2] (kg/m^2), WC - Waist circumference(in cm), HC - Hip circumference(in cm), SBP - Systolic blood pressure(mmHg), DBP - Diastolic blood pressure(mmHg). Hirsutism score by Ferriman Gallwey score (cut off ≥8). * - significant difference, ** - highly significant difference

We observed the prevalence of T2DM and prediabetes were 13.3% (4 cases) and 6.6% (2 cases) in obese PCOS women respectively. But the prevalence of T2DM and prediabetes were 10% (3 cases) and 16.6% (5 cases) in overweight PCOS women respectively.

We could found among PCOS women that 7 cases (23.3%) were prediabetes with regarding FBS >100 mg/dL but among control, we noticed only one (3.3%) had prediabetes.

We detected 23.3% (7 cases) had MS among newly diagnosed PCOS cases than the control group (0%) in our study (Abdominal obesity WC ≥ 88 cm and any of two of the following: TGL >150 mg/dL, HDL- C < 50 mg/dL, BP >130/85 mmHg, FBS >100 mg/dL, IR).

Table V Metabolic data mean of PCOS cases and controls and their significance

| S.No. | Parameters | MEAN | | 't' value | p value |
		CASES (n = 30)	CONTROLS (n = 30)		
1.	FBS	89.23±13.92	88.47±7.66	0.264	0.792
2.	Hb	14.16±1.75	11.5±0.95	0.929	0.357
3.	HbA$_{1C}$	6.03±1.03	5.35±0.43	3.364	**0.002***
4.	TGL	134.53±58.15	106.8±36.31	2.216	**0.031***
5.	T-C	180.6±35.1	174.2±31.82	0.740	0.462
6.	HDL-C	46.17±9.6	44.87±6.4	0.615	0.541
7.	LDL- C	106±27.8	109.47±25.7	-0.501	0.619
8.	VLDL-C	27.67±11.6	20.20±8.0	2.881	**0.006***

FBS- fasting blood sugar(mg/dL), Hb- total hemoglobin (g/dL), HbA$_{1C}$ – Glycated hemoglobin(%), TGL- triglycerides(mg/dL), T-C- total cholesterol(mg/dL), HDL-C- high density lipoprotein cholesterol (mg/dL), LDLC- low density lipoprotein cholesterol (mg/dL) & VLDL-C- very low density lipoprotein cholesterol (mg/dL). * - significant difference, **- highly significant difference.

Table VI Hormonal data mean of PCOS cases and controls and their significance

| S.No. | Parameters | MEAN | | 't' value | p value |
		CASES (n = 30)	CONTROLS (n = 30)		
1.	FSH	6.79±2.9	11.31±26.1	-0.942	0.350
2.	LH	12.72±8.99	7.02±6.2	2.828	**0.006***
3.	LH / FSH ratio	2.25±2.3	1.01±0.72	2.751	**0.008***
4.	PRL	15.20±9.27	8.6±4.91	3.446	**0.001****
5.	T.Testo	47.85±23.55	22.5±11.93	5.256	**0.000****
6.	FT	10.298±17.08	1.842±1.39	2.702	**0.011***
7.	DHEAS	2.272±1.4	2.074±0.58	0.716	0.477
8.	DHEAS / FT ratio	0.815±0.95	1.922±1.53	-3.347	**0.001****
9.	ESTRONE	209.29±316	97.23±6.96	1.942	0.057
10.	TSH	2.2±0.9	2.35±0.7	-0.657	0.514

FSH – Follicular Stimulating Hormone (2.5-10.2 mIU/mL), LH - Luteinizing Hormone(1.9 -12.5 mIU/mL) , PRL – Prolactin (2.8-28.2 ng/mL), T.Testo- Total Testosterone (14- 76 ng/mL),FT- Free Testosterone (0.01-7.01pg/dL), DHEAS-dehydroepiandrosterone sulfate(0.46-2.75µg/mL), ESTRONE (25-350pg/mL) & TSH- Thyroid Stimulating Hormone(IU/mL) * - significant difference, ** - highly significant difference

DISCUSSION

Polycystic ovary syndrome (PCOS) is the most prevalent endocrinopathy in reproductive women with ovulatory dysfunction, hyperandrogenism and IR with high potential for diabetes mellitus (T2DM), obesity and cardiovascular disease and metabolic syndrome (MS).

PCOS patients were identified by Rotterdam criteria- any2 out of 3

- Oligo-ovulation or anovulation
- Clinical or biochemical signs of hyperandrogenism,
- Polycystic ovaries by Ultrasonography

The prevalence of obesity in the PCOS population ranges from 38% to 87%. Obesity is associated with insulin resistance.[6] Many women with PCOS have insulin resistance, but insulin resistance in PCOS is not dependent on obesity. It had been reported that in obese women with PCOS, the prevalence of insulin resistance was higher than obese women with normal menstrual cycle in the control group.[7]

PCOS patients are at higher risk for the metabolic syndrome which includes dyslipidemia, Type2 diabetes mellitus (T2DM), hypertension and obesity. In a study of 254 women with PCOS, the prevalence of impaired glucose tolerance was 31% compared with 10.3% in controls, and the prevalence of T2DM was 7.5 % compared with 1.5% in controls.[8]

Obese PCOS women showed a SAT (Subcutaneous Adipose tissue Topography) Top pattern very similar to that of women with T2DM. The SAT of the obese PCOS patients was strongly shifted into the android direction, appearing as "super-apples" with significantly increased upper trunk obesity to 237.8% and a significantly decreased leg SAT development to 79.8% than healthy controls.[9]

Increased SAT layers on the trunk are associated with insulin resistance, impaired glucose tolerance which can lead to deranged lipid profile in women suffering from PCOS.[10]

Though we had done this study with other parameters like fasting glucose, HbA$_{1c}$, relevant hormones with statistically significant difference, we are concerned with LAP index and comparison with BMI, BAI and W/H ratio. The LAP index, an ordinal scale combining WC and triglycerides, was first tested in 2005 in a study using data from National Health and Nutrition Examination Survey sample database (NHANES III). The authors compared the LAP index to BMI in terms of ability to identify cardiovascular risk in adults.[1]

The WC (estimated population minimum 65 cm for men and 58 cm for women) and TG concentration from the third National Health and Nutrition Examination Survey (N = 9,180, statistically weighted to represent 100.05 million US adults) were used to compute a "lipid accumulation product" and to describe the population distribution of LAP. LAP and BMI were compared as categorical variables and as log-transformed continuous variables for their ability to identify adverse levels of 11 cardiovascular risk factors. As continuous variables, LAP provided a consistently more adverse beta coefficient (slope) than BMI for nine cardiovascular risk variables (p < 0.01)[3]

LAP is based on a combination of two measurements that are safe and inexpensive to obtain. The first is waist circumference

(WC), a measure of truncal fat that includes the visceral (intra-abdominal) depot. The other is the fasting concentration of circulating triglycerides (TG), the esterified, long-chain fatty acids that circulate through blood contained stably inside lipoproteins. Both waist size and TG concentration tend to rise with age and it was suggested that their values are tend to increase over time. Waist size and circulating TGs are robustly associated with insulin resistance, triglyceridemia and increase the cardiovascular disease risk.[3]

In another study, Italian men and women with diabetes were followed for two years after randomization to a physical activity counselling intervention. Across six levels of aerobic energy expenditure, those who exercised more experienced significant reductions (p < 0.001) in waist circumference and circulating TG, but no reductions (p > 0.25) in either weight or BMI. Thus, they found that the participants in both of these studies would have achieved a substantial reduction in LAP in association with improved cardiovascular risk factors, but their reduction in BMI was modest and less clearly associated with cardiovascular benefit. These observations from Asia and Europe demonstrate a potential advantage to using LAP as an intermediary variable by which to assess interventions against obesity-related risk.[3]

LAP showed the highest prediction accuracy among adiposity measures with an area under the ROC curve (AUC) of 0.901. This was significantly higher than the adiposity measure of waist-to-height ratio (AUC 0.813). LAP had significantly higher predictability than other adiposity measures tested. The LAP method was shown to predict diabetes and recognize cardiovascular risk better than body mass index (BMI) in previous studies. LAP is a simple indicator that requires only the determination of circulating triglycerides and measurement of waist circumference. The disadvantage of measuring the waist circumference which is not able to differentiate between visceral adipose tissue and subcutaneous adipose tissue.[1]

Visceral adiposity is more strongly associated with cardio metabolic risks compared with subcutaneous adipose tissue. Visceral adipose tissue adipocytes have a higher rate of lipolysis and also produce more adipocytokines, such as interleukin-6 and plasminogen activator inhibitor-1. Therefore, it is important to include a routinely applicable indicator for evaluation of visceral adiposity. Triglyceride has been reported as a significant correlate of visceral adipose tissue in healthy men, even after controlling for abdominal subcutaneous adipose tissue. Furthermore, the use of triglyceride levels in combination with waist circumference, termed hypertriglyceridemic waist, has been shown to be able to identify individuals with the greatest amount of visceral fat and to be associated with increased risk of MS, diabetes, and coronary artery disease .[11]

LAP index is highly correlated with HOMA (Homeostatic Model Assessment) index in PCOS patients.[1] In present study, we observed that LAP score were increased in those who had BMI > 25 kg/m2. As LAP score is considered as a marker of cardiovascular risk, IR and MS. We could conclude that the prevalence of MS in PCOS patients is more common than controls and also they were more prone for type 2 diabetes mellitus and increased coronary artery disease. Therefore, we could suggest clinicians in decision-making for treatment with

insulin-sensitizers for those patients having LAP score of > 34.5.[1]

CONCLUSION

In conclusion, LAP index can be considered as a reliable, cheap marker of cardiovascular risk, IR and MS. The early detection and intervention can be possible to prevent metabolic and clinical complications among PCOS patients by LAP scoring. Monitoring LAP score while intervention, can be considered as an advantageous in reducing morbidity and mortality in PCOS patients.

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