

Original article:

Association of insulin resistance in lean and non - lean women with polycystic ovarian syndrome

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ABSTRACT

Background: one of the most common endocrine disorder of reproductive age group is POLYCYSTIC ovary syndrome (PCOS) ,prevalence of which has been reported to range from 2.2% to 26 % of women in their reproductive years. obesity and insulin resistance are closely linked to development of pcos and its clinical features

Methods: a prospective study was done. Fifty three PCOS women were divided into two groups: Group A –lean (B.M.I 18- 24 kg/m²) and Group B -non lean (B.M.I > 24kg.m²). ,serum fasting insulin and HOMA- IR were compared between these groups.

Results : 21.73% of lean PCOS and 40% of nonlean PCOS patients have hyperinsulinemia.. and 34.78% of lean pcos and 56.66 % of non lean pcos had insulin resistance based on HOMA IR calculation. But the differences between them were not statistically significant. but, with BMI, fasting insulin value and HOMA-IR showed a significant positive correlation .

Conclusions: irrespective of BMI ,PCOS both lean and non lean patients are vulnerable to the hazards of insulin resistance and there is a positive correlation of BMI with insulin resistance

Keywords:. Lean PCOS, non lean PCOS, Fasting Insulin, HOMA-IR

Introduction:

one of the most common endocrine disorder of reproductive age group is POLYCYSTIC ovary syndrome (PCOS)-1 ,it is characterized by presence of, menstrual dysfunction (oligomenorrhea or heavy menstrual bleeding) , infertility , polycystic ovary and clinical hyperandrogenism (hirsutism and /Or acne)or biochemical hyperandrogenism (Elevated androgens)—2. The Rotterdam criteria for diagnosis of pcos requires the presence of two out of three of the following : a)oligo/ anovulation, b) clinical/or biochemical hyperandrogenism or c)polycystic ovaries on ultrasound—3&4 . Globally prevalence estimates of pcos are highly variable ranging from 2.2% to as high as 26% -5.obesity and insulin resistance are closely linked to development of pcos and its clinical features—6 insulin resistant is seen in pcos women, and this hyperinsulinemia plays a role in the pathogenesis of the reproductive disturbances -(7). A study by Yildizhan et al conducted on 100 lean women with PCOS found that 47% were insulin resistant. This shows the need for evaluating both non lean and lean women with PCOS as its prevalence is high and to prevent the reproductive, metabolic and cardiovascular consequences-8. Over time, an imbalance in the relationship between glucose and insulin and, without treatment, may eventually cause health complications affecting various parts of the body. Predicting insulin sensitivity in normoglycemic individuals is important, as

intervention programs are more likely to be successful at this stage rather than after the development of impaired glucose tolerance. –9,

fasting insulin alone was as accurate at predicting insulin resistance in the normoglycemic population as HOMA, insulin-to-glucose ratio, and the Bennett index—9 , Laakso et al showed that fasting insulin had less variability and has higher correlation with insuline sensitivity index (ISI) normoglycemic individual than with individuals with diabetes and impaired glucose tolerance (IGT)-(10). Thus, various method to predict insulin sensitivity in normoglycemic individuals should be compared with fasting insulin .

euglycaemic hyperinsulinaemic clamp technique is considered the gold standard in the assessment of insulin resistance -[11], this method is too cumbersome for standard clinical practice. Hence, several other methods have been designed including a homeostatic (HOMA) model based on fasting glucose and fasting insulin ($HOMA-IR = [glucose] (mmol/l) \times [insulin] (\mu U/ml) / 22.5$)- [12] other methods to diagnose insulin resistance in a research setting are costly ,time,& labor, consuming and are not feasible for large populations or routine interval assessment of individuals at risk.

Therefore identifying the PCOS women who are insulin resistant with a simple test may become more relevant as therapeutic interventions may improve insulin sensitivity in PCOS. We therefore intend , to compare insulin resistance (IR) by HOMA-IR evaluation & fasting insulin in non lean and lean with polycystic ovary syndrome.

Subjects and Methods

OPD of Padmashree Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune in July 2018. 53 patients of PCOS were included in the study. With prior consent and approval from patient and ethical committee, patients were given a questionnaire which included the information regarding age, height, weight, BMI and waist circumference. It also included information regarding menstrual symptoms like menstrual cycle regularity, oligomenorrhoea, high menstrual bleeding, amenorrhoea, blood pressure measurement, markers of metabolic syndrome and presence of insulin resistance, past history and family history, was evaluated .

Inclusion criteria

- clinical and /or Biochemical hyperandrogenism
- Oligomenorrhoea-Amenorrhoea
- PCO feature in USG.

Exclusion criteria

- thyroid dysfunction
- cushing syndrome, Hyperprolactinemia,
- Congenital adrenal secreting tumour,
- Patients with suspected of androgen secreting tumour,
- diagnosed diabetic patient

BMI was calculated using the formula: $[weight/height^2; (kg/m^2)]$. The women had a body mass index greater than 18 but upto 24 kg/m² were in group A (lean group) . women with body mass index greater than 24 kg/m² in group B(non lean group). All women were in age group between 12–45 yr .. The diagnosis of PCOS was made by the finding of classical history and ultrasound findings .

Study protocol

A predesigned structured questionnaire was prepared based on the literature on pcos it was used for data collection and bmi calculation was done among participants.

All blood studies were performed after a 3-day 300-g carbohydrate diet and an overnight fast., and blood was obtained for glucose and insulin level estimation by venipuncture in left arm

These tests were performed without regard to the phase of the menstrual cycle.

Assays

1)A single fasting blood sample obtained and insulin levels were measured by Chemiluminescent Microparticle Immuno Assay (CMIA). 2)The glucose oxidase–peroxidase method was used for measurements of plasma glucose.3) Insulin resistance (IR) was calculated by using the HOMA model [HOMA-IR=fasting serum insulin(μ U/L) x fasting plasma glucose (mmol/L)/22.5]. HOMA-IR value more than 2.5 was considered as insulin resistance. normal values were considered as Fasting Insulin (2.6-24.9 μ U/mL). Fasting BSL (70-100)mg/dL.

Data analysis & Statistical Analysis

Data management and analysis was done using Microsoft excel and Epi-info software and socscistatistics. The frequency distribution and graph were prepared for the variables. The variables were assessed using chi-square with Yates correction. The test was considered significant only if the p value comes out to be less than 0.05.

Results

Table I. Distribution of Cases According to Age Groups

| Age Group (In years) | Frequency | Percent |
|-------------------------|-----------|---------|
| 16-20 | 10 | 18.86% |
| 21-25 | 29 | 54.71% |
| 26-30 | 13 | 24.52% |
| 36-40 | 1 | 1.88% |
| total | 53 | 100% |

Out of 53 total cases, majority of the PCOS group of patients were aged between 21-25 years, 10 patients were adolescent PCOS (18.86%).

Table II. Distribution of Cases According to Type (lean/nonlean)

| type | frequency | percent |
|----------|-----------|---------|
| lean | 23 | 43.396% |
| Non lean | 30 | 56.603% |
| total | 53 | 100% |

Table III. Mean Values for Various Physical and Biochemical Indices PCOS Case

| variables | N | Minimum | Maximum | Mean | Standard deviation |
|-------------------------------|----|---------|---------|--------|--------------------|
| BMI (kg/m ²) | 53 | 20.00 | 36.80 | 26.85 | 4.997 |
| Fasting Insulin (μ U/mL) | 53 | 2.00 | 41.44 | 16.638 | 11.663 |
| Fasting BSL (mg/dL) | 53 | 72 | 112 | 88.622 | 8.921 |

Table IV. Fasting insulin level

| | Fasting insulin level >24.9 μU/mL | Fasting insulin level <24.9 μU/mL | Margin row total |
|---------------------|--------------------------------------|--------------------------------------|---------------------|
| Non lean | 12 | 18 | 30 |
| lean | 5 | 18 | 23 |
| Margin column total | 17 | 36 | 53 |

The chi-square statistic is 1.9926. the p-value is 0.158. not significant at p<0.05

The chi-square statistic with yates correction is 1.2426. **the p- value is 0.264**, not significant at p<0.05

Table V. HOMA-IR (Homeostatic model assessment and insulin resistance)

| | HOMA-IR >2.5 | HOMA-IR <2.5 | total |
|----------|--------------|--------------|-------|
| Non lean | 17 | 13 | 30 |
| lean | 8 | 15 | 23 |
| | 25 | 28 | 53 |

The chi-square statistic is 2.502 the p-value is 0.1137. not significant at p<0.05

The chi-square statistic with yates correction is 1.7009. **the p- value is 0.192176**. not significant at p<0.05

Table VI. Correlation with BMI.

| B.M.I | | |
|------------------|-------------------------|-----------------------|
| HOMA-IR | NUMBER | 53 |
| | PEARSONS CORRELATION | 0.3718 |
| | (2 TAILED) SIGNIFICANCE | (29.5411) SIGNIFICANT |
| FASTIING INSULIN | NUMBER | 53 |
| | PEARSONS CORRELATION | 0.2388 |
| | (2 TAILED) SIGNIFICANCE | (5.847) SIGNIFICANT |

Discussion

In the present study, 21.73% of lean PCOS and 40% of non lean PCOS patients have hyperinsulinemia. And p value is not < 0.05 so There is NO significant statistical difference between both groups (TABLE 4). And there is a significant positive correlation of fasting insulin with BMI (TABLE 6) Silfen et al. reported more than 2-fold increase in FI levels and a significant decrease in estimations of insulin sensitivity in overweight as compared to normal weight adolescents with PCOS. -(13) Yildirim et al reported higher FI levels in non-obese PCOS women as compared to the normal controls-(14) In this present study 34.78% of lean pcos and 56.66 % of non lean pcos had insulin resistance based on HOMA IR calculation and p value is not < 0.05 so there is NO significant statistical difference between both groups (TABLE 5). And there is a significant positive correlation of HOMA-IR with BMI (TABLE 6) Gupta et al in their study noticed a higher IR between both obese and non-obese PCOS (44% and 36%) as compared to normal controls.-(15) Alebic MS et al ,reported 57% of overweight/obese women with PCOs were insulin resistant, while in lean patients group the prevalence was 9.3 %. And also insulin sensitivity (IS) was reduced 50% in obese PCOs from that in lean controls - (16).

In a follow-up study by Ramezani done on 637 subjects, a higher prevalence of IR was noted among PCOS women Both obese and lean category, PCOS is a risk factor for insulin resistance -(17). It's better to evaluate insulin resistance during PCOS evaluation to prevent long-term complications. In a study by Jayashree S et al, found HOMA-IR of ≥ 2.5 , indicating insulin resistance, was found in 38.3% of lean PCOS and 51.7% of obese PCOS patients. The difference is not statistically significant but there is a significant positive correlation of HOMA-IR and fasting insulin with BMI. -(19)

In a study by Morales et al they reported that insulin sensitivity reduced by 50% in lean PCOS as compared to normal controls, and was further decreased in obese controls with a 2-fold greater reduction in obese PCOS than in obese controls, suggesting that IR is a common feature in PCOS, and that obesity is an additional component to IR in obese PCOS. -(18)

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