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Research Article

Indices For Detecting Insulin Resistance

# The Value of Insulin Resistance indices For detecting Insulin Resistance in Polycystic Ovarian Syndrome Patients

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**Abstract:** Polycystic Ovarian Syndrome (PCOS) is characterized by increased ovarian and androgen hormone secretion. Patients with PCOS are said to be at high risk for insulin resistance(IR). IR is a sign of PCOS that comprises impaired glucose tolerance and elevated insulin production. HOMA-IR is a test that assesses insulin resistance by measuring blood glucose and insulin levels. There are other indexes that are also available for determining IR such as the quantitative insulin sensitivity check index(QUICKI) and McAuley index. Hence, in this study HOMA-IR, QUICKI and McAuley index were used to determine the IR among PCOS individuals. This case-control cross sectional study included 62 participants between the age group of 20-40 years. They were divided into two groups such as Group B which includes 31 PCOS patients diagnosed based on Rotterdam criteria and Group A includes 31 healthy age-matched female participants. After obtaining informed consent, fasting blood sample was collected from all the participants. Based on the analyzed biochemical parameters IR was assessed using HOMA-IR, QUICKI and McAuley index. For statistical analysis student t-test, ROC curve and bivariate regression analysis were done. In this study, it is observed that an increase in BMI was at a higher risk of developing PCOS. It is seen that fasting glucose, insulin and lipid profile (except HDL-C) were significantly elevated in PCOS individuals. The HOMA-IR was significantly increased and QUICKI and McAuley's index were significantly decreased in PCOS which shows that PCOS patients are at higher risk of developing IR. Crude odds were calculated which shows that increase in HOMA-IR levels has an 86.25% increase risk of developing IR in PCOS patients when compared with the other indexes.HOMA-IR has a higher predictor % of developing IR in PCOS individuals, but still QUICKI and McAuley index can also be used as a predictor of risk.

**Keywords:** HOMA- IR, Insulin Resistance, McAuley Index, QUICKI and PCOS.

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## 1. INTRODUCTION

PCOS is a prevalent endocrine issue that impacts 4–7% of women of reproductive age.[1] Females have a stressful experience and gynaecologists have a difficult multiplex syndrome. PCOS prevalence varies widely over the world, ranging from 2.2 percent to 26 percent of people in the 18-40 age group, depending on how it is defined. These differences exist due to difficulties in evaluating hormones and a lack of policy on diagnostic criteria.[2] The revised Rotterdam 2003 criteria are the most commonly used diagnostic criteria for PCOS.[3] The etiology and pathophysiology of PCOS, on the other hand, remain unknown, and various risk factors including genetics, environment, nutrition, lifestyle, and others are still being researched. The symptoms and severity of the disorder vary, but the majority have central obesity or android fat deposition (fat at the abdominal wall and viscera). Insulin resistance is relatively high in Android fat accumulation.[4,5]
PCOS is characterized by increased ovarian and androgen hormone secretion, as well as clinical characteristics such as acne, hirsutism, alopecia, irregular menstruation cycles, and different types of cysts in the ovaries. Insulin resistance (IR) is a sign of PCOS that comprises two conditions: impaired glucose tolerance and elevated insulin production (Hyperinsulinemia).[6] Patients with PCOS are said to be at high risk for IR.[7] IR occurs when the human body's reaction to insulin is reduced. Clinical and/or biochemical hyperandrogenism, acne, hirsutism, alopecia, oligomenorrhoea/amenorrhea, and/or polycystic abnormalities in the ovaries proven by ultrasonogram (USG)[8] are all relevant symptoms as per Rotterdam criteria. Preeclampsia, intrauterine death (IUD), and endometrial cancer are all more likely in women with PCOS. Furthermore, evidence suggests that due to the relationship between PCOS and IR, PCOS patients are more likely to acquire Type 2 diabetes, dyslipidemia, systemic hypertension, and heart illness. As a result, glucose in the blood is held back from being absorbed by cells, resulting in glucose intolerance. In practice, people with insulin resistance have more insulin hormone in their blood. Because insulin is unable to execute its function properly, blood glucose levels rise. Homeostatic model assessment of insulin resistance(HOMA-IR) is a test that assesses insulin resistance by measuring blood glucose and insulin levels in people who are fasting. This examination can also be used to determine insulin resistance, which has an advantage over OGTT in that the person receiving the test just has to draw blood once. It could be useful for screening. There is still no conclusion based on previous research. HOMA-IR greater than 2.5 was used by Matthews et al. to diagnose insulin resistance in the general population.[9] The precise cut-off value utilized in diagnosing insulin resistance is not available in HOMA-IR. As a result, the objective of this paper was to establish the results of employing QUICKI and McAuley index as a diagnostic test for detecting insulin resistance(IR) and glucose intolerance in women with PCOS, as well as to define the suitable cut-off value for diagnosing IR, glucose intolerance and to generate valuable data for medical practice. Our aim and objective is to determine INSULIN RESISTANCE by using HOMA-IR[9]; Quantitative insulin-sensitivity check index (QUICKI)[10]; McAuley index[11]; and glucose intolerance among patients with PCOS.

## 2. MATERIALS & METHODS

### *2.1 Study Design, Variables and Parameters*

***Study Type***

Case control study

***Duration of Study***

July 2021 to Jan 2022

***No of Study Groups***

Two- Group A & Group B

***Group-A***

Control group - will consist of age and sex matched control

***Group-B***

Study group - Patients of age group 20-40 years diagnosed with PCOS will be taken as group B.

### *2.2 Sample Size*

Sample size was calculated as 62 in both control and study group with the help of the statistician, based on the study conducted by Vidya Bharathi et al.,an epidemiological survey: Effect of predisposing factors for PCOS urban and rural population year 2016.[12]

### *2.3 Formula*

$$n = \frac{z^2(pq)}{d^2}$$

**z = 1.96 (Type I error)**
**p = 0.089 ( Proportion of population )**
**q = 1- p (1- 0.089)**
**= 0.911**
**d = 10% ( Degree of accuracy)**
**= 0.1**
**n = 31**

### *2.4 Ethical Clearance*

The study protocol was carried out with the approval of the Institutional ethical committee (ECN: 2866/IEC/2021), and all subjects gave their informed written consent.

### *2.5 Inclusion Criteria*

Patients diagnosed with PCOS under the age group of 20-40 years with

1. Irregular menstruation
2. Infertility
3. Presence of Polycystic ovaries on ultrasonogram scans

### *2.6 Exclusion Criteria*

1.Patients with clinical conditions that will affect insulin levels like thyroid disorder, pregnancy or lactating women, renal diseases, h/o oral contraceptives, cushing's syndrome, hypertension and cardiovascular diseases. 2. Age group less than 20 years and more than 40years.

### *2.7 Sample Collection and Separation*

Venous blood sample (5ml) was collected from anterior cubital vein after overnight fasting of 10-12 hours in a appropriate vacutainer tube. Serum was separated from collected blood samples by centrifugation at three thousand (3000) rpm for ten minutes and serum was subsequently utilized for measurement of glucose, total cholesterol, triglyceride, LDL-C and HDL-C using Beckman Coulter Auto – analyser (AU-480). Serum insulin was analysed in VITROS Eci immunoanalyzer. HbA1c was analysed in BIORAD D10 machine (HPLC)

**TABLE: 1 - BIOCHEMICAL PARAMETERS WITH METHODOLOGY**

| PARAMETERS | METHODOLOGY | INSTRUMENTS |
|---|---|---|
| Fasting Plasma Glucose (mg/dl) | Hexokinase | Beckman Coulter AU480 auto analyzer |
| Insulin | ECLIA | VITROS Immuno analyzer |
| Total cholesterol (mg/dl) | Cholesterol oxidase | Beckman Coulter AU480 auto analyzer |
| Triglycerides (mg/dl) | Glycerol oxidase | Beckman Coulter AU480 auto analyzer |
| HOMA-IR | Fasting Glucose X Fasting Insulin /405 | Calculation |
| QUICKI | 1/[log insulin (μU/mL) + log glucose (mg/dL)] | Calculation |
| McAuley index | Exp [2.63-0.28 ln (fasting serum insulin (IU/mL)]-0.31 ln [serum TG (mmol/L)]} | Calculation |
| HDL-C (mg/dl) | Direct method | Beckman Coulter AU480 auto analyzer |
| LDL-C (mg/dl) | Direct method | Beckman Coulter AU480 auto analyzer |
| VLDL-C (mg/dl) | (TG/5) | Calculation |

## 3. STATISTICAL ANALYSIS

The data were analyzed using the software SPSS (25.0). The data were represented as mean and standard deviation. The student t-test was used to compare the mean difference between the groups. Bivariant regression analysis was used to calculate the crude odds ratio with a 95% of confidential interval. For all the statistical test p values < 0.05 was taken as significant. The graph was plotted using excel.

## 4. RESULTS

### 4.1 *Socio-Demographic Profile Of The Study*

A total of 62 subjects were studied 31 subjects diagnosed with polycystic ovary syndrome(PCOS) were in the case group and 31 healthy subjects were in the control group. The mean age of controls and cases were 23.77± 3.42 years and 25.32 ± 3.87 years respectively age range of 20-40 years. The data were distributed according to the age group, as 20-25 years (with 90% control and 58% cases), 26-30 years (7 % control and 39% case), 31-35 years (0% control and 0% case) and 36-40 years (3% control and 3% case) Table 2.

**TABLE 2: Distribution of Subjects based on age group**

| AGE | CONTROL (Group A) | | CASE (Group B) | |
|---|---|---|---|---|
| | Number of subjects | Percentage | Number of subjects | Percentage |
| 20-25 | 28 | 90% | 18 | 58% |
| 26-30 | 2 | 7% | 12 | 39% |
| 31-35 | 0 | 0% | 0 | 0% |
| 35-40 | 1 | 3% | 1 | 3% |
| Total | 31 | 100% | 31 | 100% |
| Mean ± SD | 23.77±3.42 | | 25.32±3.87 | |

The mean BMI (Kg/m2) for. control (23.07 ± 1.51) and case (28.26 ± 6.33) were calculated and found there is a significant difference (p<0.0001) between the mean levels of case and control. The data were distributed according to their BMI as normal (18.5-22.9), overweight (23-24.9), obese (≥ 25) "patients according to the Asian criteria, in which 48% normal, 48% overweight and 4% obese in control and 10% normal, 16% overweight and 74% obese case subjects were found in control and case group respectively(Table:3). The values are statistically significant if *p value < 0.05.

| TABLE 3 : Distribution of Subjects according to BMI | | | | | |
|---|---|---|---|---|---|
| BMI ($Kg/m^2$) | Control | | Case | | P value |
| | Number of subjects | Percentage | Number of subjects | Percentage | |
| **Normal** | **15** | **48%** | **3** | **10%** | |
| **Overweight** | **15** | **48%** | **5** | **16%** | |
| **Obese** | **1** | **4%** | **23** | **74%** | <0.0001*** |
| **Total** | **31** | **100%** | **31** | **100%** | |
| **Mean ± SD** | 23.07 ± 1.51 | | 28.26 ± 6.33 | | |

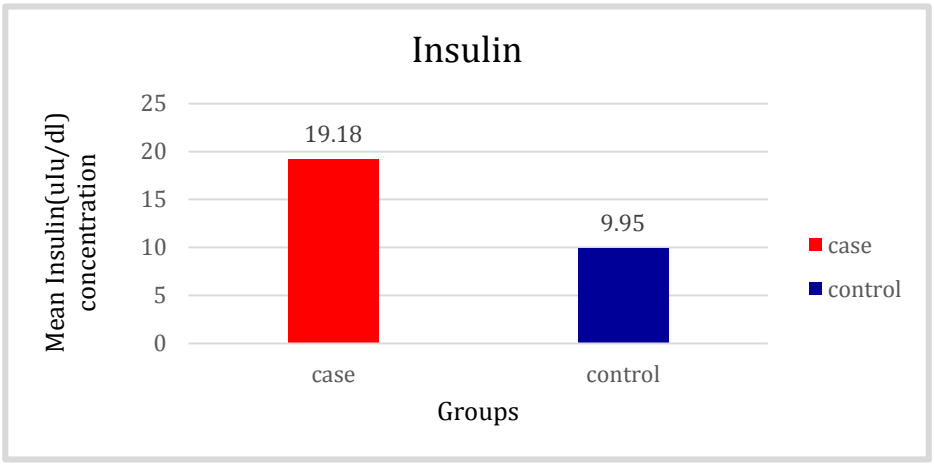
***The values are statistically significant if *p value < 0.05.*** <0.001***

### *4.2 Student's T Test Analysis of Variables*

The mean values of Insulin, HOMA-IR, QUICK index, McAuley index, fasting blood glucose, total cholesterol, triglyceride, HDL-C, LDL-C, and VLDL-C were compared between the PCOS patients and healthy subjects with the help of student's t-test. Insulin, HOMA-IR, QUICK Index, McAuley index, fasting blood glucose, total Cholesterol, Triglyceride, LDL-C, and VLDL-C were found to be statistically significant and HbA1c, HDL-C were not significant. (Table-4) (Fig: 1-4) The values are statistically significant based on the p value.* p value < 0.05,

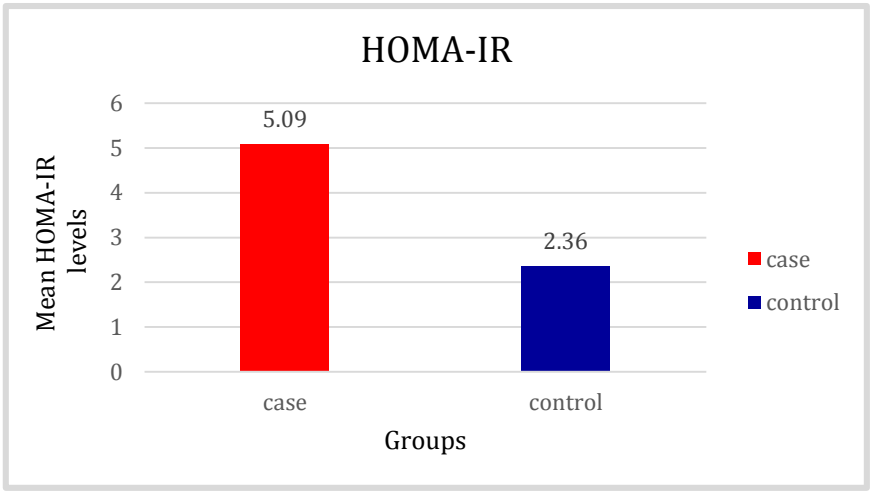
| TABLE 4: Comparison of Mean ± SD of the Measured Biochemical Parameters between the PCOS Patients (Group B) and Healthy Subjects (Group A). | | | |
|---|---|---|---|
| **PARAMETER** | **Control (Group A) Mean ± SD** | **CASE(Group B) Mean ± SD** | **p value** |
| **Insulin(ulu/dl)** | 9.95 ±4.87 | 19.18 ±8.95 | < 0.0001*** |
| **HOMA-IR** | 2.36±1.19 | 5.09±2.42 | < 0.0001 |
| **QUICKI index** | 0.34 ± 0.02 | 0.30 ± 0.02 | <0.0001*** |
| **McAuley index** | 4.99 ±0.85 | 3.86 ± 0.7 | < 0.0001*** |
| **Fasting blood glucose (mg/dl)** | 95.39 ±4.49 | 107.26 ±6.04 | < 0.0001*** |
| **T-Cholesterol(mg/dl)** | 152.71 ±17.89 | 175.16 ±28.55 | 0.0005*** |
| **Triglycerides(mg/dl)** | 74.10 ±25.74 | 96.90 ±44.75 | 0.0168* |
| **HDL-C(mg/dl)** | 48.87 ±7.42 | 46.61 ±10.38 | 0.32NS |
| **LDL-C(mg/dl)** | 105.84 ±15.71 | 126.19 ±26.29 | 0.0005*** |
| **VLDL-C** | 15.23 ±6.26 | 19.39 ±9.00 | 0.0388* |
| **HbA1c** | 5.28 ±0.29 | 5.35 ±0.31 | 0.36NS |

***The values are statistically significant based on the p value.* p value < 0.05,*** <0.001***



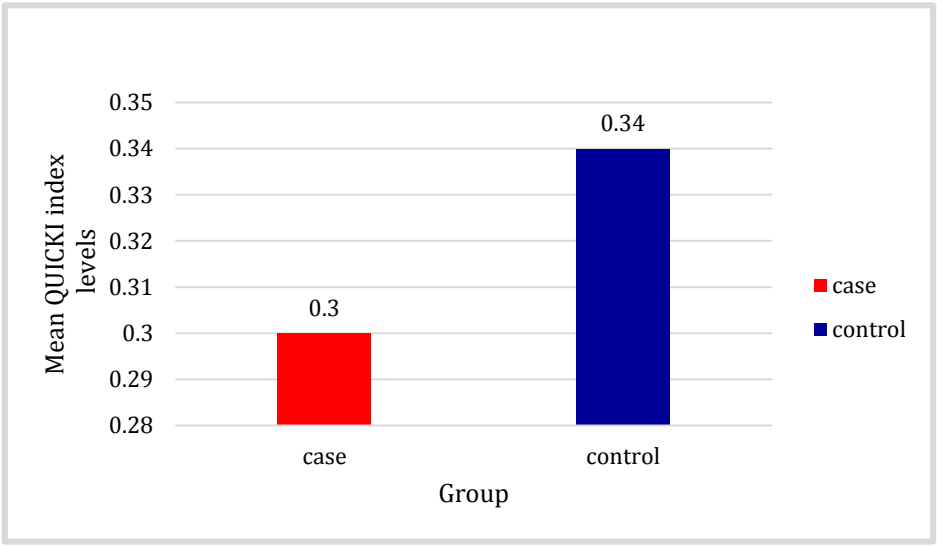

***The figure 1 shows the bar graph with the mean difference in the insulin levels among case and controls, where the mean levels of insulin among cases were higher when compared to the controls***

**Fig 1: Comparing the Mean Levels of Insulin.in Case and Control (Bar Graph).**



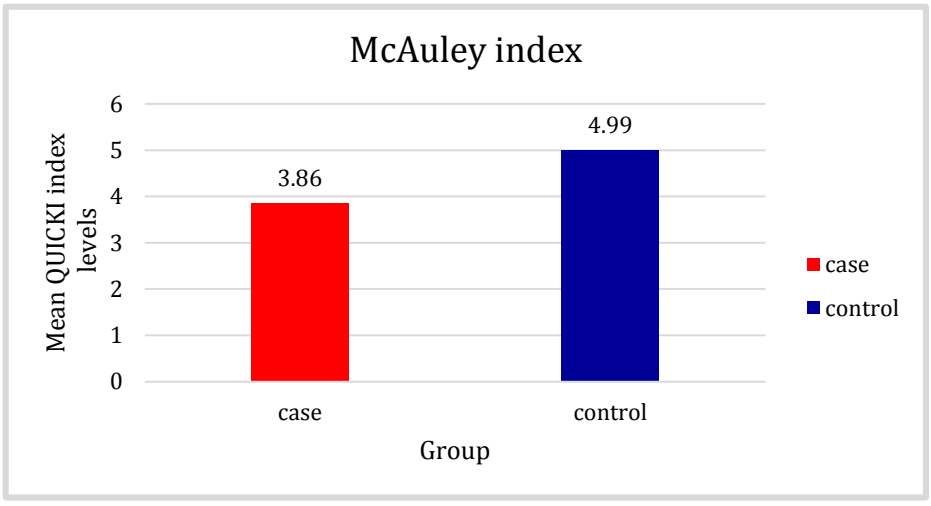

*The figure 2 shows the bar graph with the mean difference in the HOMA-IR levels among case and controls, where the mean levels of HOMA-IR among cases were higher when compared to the controls*

**Fig 2 : Comparing the Mean Levels of HOMA-IR in Case and Control (Bar Graph)**




*The figure 3 shows the bar graph with the mean difference in the QUICK index levels among case and controls, where the mean levels of QUICK index among cases were lower when compared to the controls*

**Fig 3 : Comparing the Mean Levels of QUICK Index in Case and Control (Bar Graph)**




*The figure 4 shows the bar graph with the mean difference in the McAuley index levels among case and controls, where the mean levels of McAuley index among cases were lower when compared to the controls.*

**FIG 4 : Comparing the Mean Levels of McAuley index in Case and Control (Bar Graph)**

### *4.3 Bivariant regression analysis*

Crude odd's were calculated for the HOMA-IR, QUICK Index and McAuley index. It was found that the increase in HOMA-IR has 86.25% and the decrease in QUICKI and McAuley index has 4.7% and 7.6% respectively with an increased risk of developing glucose intolerance. ROC was done for McAculey index and found that values <4.4 (AUC: 0.148, p: 0.0001, 95% CL: 0.051-2.45).

**TABLE 5: Association between high serum HOMA-IR in different group of participants**

| Variables | Case % | Control % | Total % | Odds ratio | 95% CI | P Value |
|---|---|---|---|---|---|---|
| **HIGH HOMA-IR** | | | | | | |
| **High HOMAIR** | 30(97) | 8(25) | 38(61) | **86.25** | **10.05- 739.47** | **P< 0.0001** |
| **Normal** | 1(3) | 23(75) | 24(39) | | | |

***The table 5 shows the bivariant regression analysis where crude odds was calculated as 86.25, that is PCOS with patients increase HOMA-IR are 86.25 time higher risk of developing IR.***

**TABLE 6: Association between high serum QUICK Index in different group of participants.**

| Variables | Case % | Control % | Total % | Odds ratio | 95% CI | P Value |
|---|---|---|---|---|---|---|
| **HIGH QUICK INDEX** | | | | | | |
| **Lower QUICK INDEX** | 15 (48%) | 5 (16 %) | 32 (100%) | **4.7** | **1.46-15.5** | **0.009**** |
| **Normal** | 17 (53%) | 27 (84%) | 32 (100%) | | | |

***The table 6 shows the bivariant regression analysis where crude odds was calculated as 4.7, that is PCOS patients with decreased QUICK index are 4.7 time higher risk of developing IR.***

**TABLE 7: Association between high serum McAuley index in different group of participants.**

| Variables | Case % | Control % | Total % | Odds ratio | 95% CI | P Value |
|---|---|---|---|---|---|---|
| **HIGH McAuley index** | | | | | | |
| **Lower** McAuley index | 24 (75%) | 9 (28 %) | 32 (100%) | **7.6** | **2.52-23.28** | **0.0003***** |
| **Normal** | 8 (25%) | 23 (72 %) | 32 (100%) | | | |

***The table 7 shows the bivariant regression analysis where crude odds was calculated as 7.6, that is PCOS patients with decreased McAuley index are 7.6 time higher risk of developing IR.***

## 5. DISCUSSION

The biochemical parameters of FPG, fasting insulin, HOMA-IR, QUICK index and McAuley's index as markers of insulin resistance, lipid profile parameters namely total cholesterol, TGL, HDL-cholesterol, LDL-cholesterol, and VLDL-cholesterol were analyzed and their relationship between these biochemical parameters were evaluated in 31 patients with an established diagnosis of polycystic ovarian syndrome with glucose intolerance and 31 controls without PCOS. All the participants were between the age group of 20 to 40 years. This shows that 58% of PCOS women in the case group were between the age group of 20- 25 years, when compared to the age group between 35 – 40 years , it was found that 3% of the individuals may develop PCOS at this age group. This finding is supported by the work of Harmandeep Gill et al, which shows that PCOS is common in the age group between 18-25 years.[13] Based on the anthropometric evaluation, it is found that PCOS women have a significantly greater BMI than the control group, in which about 48% of the PCOS group were overweight. According to the findings of the recent study by Saxena et al, obesity increases the risk of PCOS.[14] A student t-test was used to compare the mean difference between the two groups (group A- controls and group B- PCOS patients). This study shows that fasting lipid profile parameter analysis namely total cholesterol, triglyceride, LDL- C and VLDL – C were significantly elevated among PCOS patients compared to controls. The study by Olivier Valkenburg et al showed that the triglycerides, LDL-C and VLDL-C levels were highly elevated and HDL-C levels were decreased among PCOS patients compared to non - PCOS patients.[15] Fasting plasma glucose and insulin were also analyzed and found that their levels were significantly elevated among case groups compared to controls. A study by Amisi C et al, showed that about 35 - 80% of PCOS individuals develop insulin resistance.[16] Various methods were proposed for IR assessment, among which HOMA-IR is the well-known and increasingly used method for the evaluation of IR. Recently methods such as 1/HOMA-IR, QUICKI and McAuley's index were also suggested for evaluation of IR among type II diabetic Mellitus.[17] A study by Jirí Hrebícek et al, showed that the QUICK index can be used for the diagnosis of IR in clinical and epidemiological practice and patients with the QUICK index below 0.357 indicate greater insulin resistance.[18] On the other hand, McAuley's index is used to predict insulin resistance in normoglycemic individuals.[19,20] This study shows that HOMA-IR was significantly increased and QUICKI and McAuley's index were significantly decreased in PCOS which shows that PCOS patients are at higher risk of developing IR. Hence, in this study HOMA-IQ, QUICKI and McAuley's index were used to assess to determine which index predicts the increased risk of IR among PCOS individuals. For HOMA-IR and QUICK index a cutoff value of 1.85 and 0.37 respectively obtained from the previous study[21,18] was used to determine the risk of

developing IR among PCOS individuals. For, McAuley's index ROC analysis was used to estimate the cut-off points, the value of <4.4 (AUC: 0.148, p: 0.0001, 95% CL: 0.051-2.45) is taken as the cutoff for this study. Using the bivariant regression analysis the crude odds were calculated in this study for HOMA-IR, QUICK Index and McAuley's index, which found that an increase in HOMA-IR levels has an 86.25% increase risk of developing IR in PCOS patients and a decrease in QUICKI and McAculey's index has 4.7% and 7.6% of the risk of developing insulin resistance in PCOS patients. When comparing surrogate approaches based on fasting insulin and either fasting glucose (HOMA-IR and QUICKI) or triglycerides (McAuley Index) with IR indices obtained from glucose and insulin during an OGTT, Lewandowski et al.[22] showed that the connection between various IR indices is very varied (Belfiore, Matsuda and Stumvoll indices). They concluded that the clinical use of surrogate indicators for the assessment of IR and glucose intolerance in PCOS should be approached with caution.

## 6. CONCLUSION

By using QUICK index formulae we found more insulin resistance patients than with HOMA-IR. We suggest that the QUICK index detects insulin resistance earlier than HOMA-IR. Therefore, this study leads us to formulate more sensitive and specific clinical criteria for the detection of IR and glucose tolerance among patients with PCOS. HOMA-IR has a higher predictor % of developing IR in PCOS individuals, but still QUICK Index and McAuley index can also be used as a predictor of risk.

## 7. LIMITATION OF OUR STUDY

The study was conducted in specific group of population. One of the major limitations of this study is smaller sample size. It was a cross sectional study. A prospective, multicenter investigation is required to address these limitations.

## 8. AUTHORS CONTRIBUTION STATEMENT

All authors contributed to this article conception and design. The first draft was written by Dr.B.Gayathri. Patient information and data collection was performed by T.Dixit Sweety Saral. The statistical analysis and final draft was done by Dr.B.Gayathri , T.Dixit Sweety Saral , S.Aishwarya. The final draft of manuscript was reviewed by Dr.Renuka.P, Dr.V.M.Vinodhini, Dr.M.Anuradha. All the authors reviewed and approved the final manuscript.

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## 10. CONFLICT OF INTEREST

The authors declared none.

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