Original Article

# Study of insulin Resistance in Women with Polycystic Ovarian Syndrome Using Homeostatic Model Assessment in A Tertiary Care Hospital of Bihar

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**ABSTRACT**

***Introduction:*** Polycystic ovarian syndrome or PCOS, an endocrine condition, affects women of reproductive age group and characterized by features like irregular menstruation, hyperandrogenism and infertility. In India, the prevalence of PCOS is 6% more than the prevalence noted as compared to the global prevalence. Women with PCOS had higher risk of developing type 2 diabetes mellitus at an early age due to insulin resistance.

***Objective:*** The current study was done to estimate and compare level of insulin sensitivity among women of PCOS and control population.

***Methodology:*** The study was done by department of Biochemistry, DMCH, Laheriasarai. The study population comprised of 60 women aged 15-50 years of age of diagnosed case of PCOS in study group. In control group 60 women of same age group from attendants of patients, medical college staff were taken and women residing in Darbhanga.

***Results:*** Overall, the mean age of the study participants 27.8 ± 10.3 years. It was observed that as the age advances, value of HOMA-IR (Homeostatic Model Assessment for Insulin Resistance) level increases. Values of HOMA-IR with relation to age was compared to check for any statistical association, but no statistically significant association was noted both in the study and the control population.

***Conclusion:*** Insulin resistance is common abnormality in PCOS, but it is not the universal feature. HOMA IR allow identification of insulin resistance. The test is easy to perform and cost effective, hence allowing it to be a promising screening tool.

**Keywords:** Insulin resistance, Poly Cystic Ovarian Syndrome (PCOS), Homeostatic Model Assessment for Insulin Resistance (HOMA-IR).

## INTRODUCTION

Polycystic ovarian syndrome or PCOS, an endocrine condition, affects women of reproductive age group and characterized by features like irregular menstruation, hyperandrogenism and infertility.[1] Women with PCOS had higher risk of developing type 2 diabetes mellitus at an early age due to insulin resistance.[2] The baseline etiopathology is assumed to be functional ovarian hyperandrogenism (FOH) due to insufficient androgen production. [1] The inception of PCOS often traces back to the adolescence of the individual. These adolescents are at a higher predisposition to develop health condition like diabetes, cardiovascular disease, and impotence later on. [3] Hence it is a well-known verse that in cases of PCOS early diagnosis and treatment helps to prevent or delay the above mentioned typical long-term sequel. Prevalence of PCOS is approximately 10% globally. In India, the prevalence of PCOS is 6% more than the prevalence noted as compared to the global prevalence. [4]

Although the etiology of PCOS is not completely understood, it has been postulated that PCOS has a multifactorial causation with multiple genetic, metabolic, endocrine and environmental disturbances. [5] The mechanism of PCOS has been attributed to disrupted folliculogenesis, increased androgen synthesis and development of insulin resistance in the body where insulin has lower or effect on fat, muscle and liver metabolism. In such situations there is higher circulating insulin in the female body leading to hyperandrogenism by stimulating production of ovarian androgen and inhibiting production of hepatic serum hormone binding globulin. The current study was done to estimate and compare level of insulin sensitivity among women of PCOS and control population. The study also compares the demographic and metabolic state of the women with or without PCOS.

## METHODOLOGY

**Study site:** The present study of insulin resistance in polycystic ovary syndrome women has been carried out in the department of Biochemistry, Darbhanga medical college, Laheriasarai on clinically diagnosed women of PCOS. These cases are selected from OPD of Obstetrics and Gynaecology department of Darbhanga medical college and hospital.

**Study period:** 12 months (from March 2019 to February 2020)

**Study population:** 120 (60 cases and 60 control)

**Study design:** The study population comprised of 60 women aged 15-50 years of age of diagnosed case of PCOS in study group. In control group 60 women of same age group from attendants of patients, medical college staff were taken and women residing in Darbhanga. Clearance was obtained from the institutional ethics committee and consent forms were duly signed by the patients before inclusion in the study.

**Methodology:** Blood sugar fasting and serum insulin were done in both study and control group were taken by collecting 3ml of venous blood from antecubital vein after taking full antiseptic precautions. 1 ml of blood is transferred to fluoride tube for glucose estimation and 2ml is transferred to plain tube. Blood is allowed to clot at room temperature, then centrifuged, serum was separated and stored at 2-8 centigrade. For glucose estimation plasma was separated after centrifugation then fasting glucose was done. Estimation of serum insulin was done by ELISA based on simultaneous binding of human insulin by 2 monoclonal antibodies. Estimation of plasma glucose was done by G O D/ P O D method using colorimeter that is based on the principle that glucose is oxidized to gluconic acid and hydrogen peroxide in the presence of glucose oxidase. Hydrogen peroxide further reacts with phenol and 4 amino antipyrine by catalytic action of peroxidase to form a red colored Quinoneimine dye complex. Intensity of the color formed is directly proportional to amount of glucose present in the sample. Homeostatic model assessment of insulin resistance (HOMA IR) measures insulin sensitivity of an individual. It is calculated by fasting glucose (mg/dl) X fasting insulin (mu/ ml) and then divided by 405.

**Statistical analysis**

The data observed in this study were tabulated and inference was drawn. The range, mean value, standard deviation (SD) and p – value were statistically analyzed. The data for biochemical analysis are expressed as Mean ± SD (standard deviation). Single and paired sample test was applied to determine the significance of biochemical parameters among groups. The entire data was analyzed by statistically program SPSS 23.0

## RESULTS

The study composed of 120 female subjects equally divided in the study and the control group based on the inclusion and exclusion criteria. In both the groups, serum Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), fasting sugar and serum insulin were analyzed. [Table 1] Overall, the mean age of the study participants 27.8 ± 10.3 years. It was observed that as the age advances, value of HOMA IR level increases. Values of HOMA IR with relation to age was compared to check for any statistical association, but no statistically significant association was noted both in the study and the control population. [Table 2] It was observed that value of HOMA IR is more in over weight (1.65±0.8) than in normal weight (1.62±0.51) individuals, which is statistically insignificant in the control group, while in the study group also it was noted that HOMA IR increases as the BMI increases and there was a statistically significant association between HOMA IR and BMI was noted in the study group. [Table 3] HOMA IR value in study group is more in urban (3.471.09) than rural (3.231.11) population but the value is statistically insignificant in the study group while no such association was seen in the control group. [Table 4]

**Table 1:** Comparison of Fasting blood sugar, insulin and HOMA IR in study and control group

| Parameter | Control group Mean ± SD | Study group Mean ± SD | t Value | p Value |
|---|---|---|---|---|
| FBS (mg/dl) | 84.9 ± 9.32 | 100.21 ± 12.06 | 7.78 | < 0.05 |
| Insulin (µ IU/ml) | 7.7 ± 2.45 | 13.55 ± 3.45 | 10.6 | < 0.05 |
| Homa IR | 1.61 ± 0.52 | 3.4 ± 1.09 | 11.48 | < 0.05 |

**Table 2:** HOMA IR in relation to age in the study and the control group

| Age (years) | Group | No. of cases | Range | Mean ± SD |
|---|---|---|---|---|
| <20 | Study | 10 | 0.45 - 1.92 | 1.42 ± 0.49 |
| | Control | 08 | 1.88-4.8 | 3.44±1.21 |
| 21-40 | Study | 41 | 0.22 - 2.72 | 1.60 ± 0.55 |
| | Control | 43 | 2.03-5.16 | 3.73±0.96 |
| 41-60 | Study | 3 | 0.71 - 2.53 | 1.62 ± 0.59 |
| | Control | 7 | 1.84-4.6 | 3.23±1.04 |

**Table 3:** HOMA IR in relation to BMI in the study and the control group

| BMI (kg/m²) | Group | No. of cases | HOMA IR Range | HOMA IR Mean ± SD |
|---|---|---|---|---|
| <25 | Study | 56 | 0.22-2.56 | 1.62 ± 0.51 |
| | Control | 16 | 1.66-5.16 | 2.73±1.02 |
| 25-29 | Study | 4 | 0.85-2.72 | 1.65 ± 0.8 |
| | Control | 20 | 1.12-4.72 | 3.46±1.02 |
| ≥ 30 | Study | nil | - | - |
| | Control | 24 | 1.46-5.12 | 3.8±1.02 |

**Table 4:** HOMA IR in relation to place of residence in the study and the control group

| Place of residence | Group | No. of cases | HOMA IR Range | HOMA IR Mean ± SD |
|---|---|---|---|---|
| Rural | Study | 56 | 0.22-2.56 | 1.62 ± 0.51 |
| | Control | 42 | 1.46-5.16 | 3.47±1.09 |
| Urban | Study | 4 | 0.85-2.72 | 1.65 ± 0.8 |
| | Control | 18 | 1.12-5.1 | 3.23±1.11 |

## DISCUSSION

PCOS is having various short- and long-term consequences on women health. Women affecting PCOS showing increased prevalence of infertility and menstrual irregularity. Long term consequences of PCOS are type II diabetes, hypertension, dyslipidemia and cancer. Insulin resistance has prognostic marker in PCOS. The normal range of HOMA IR varies from laboratory to laboratory. In the current study, mean HOMA IR is 1.61±0.52 in the study group which is similar to study done by Gurushankar Govind R et al in 2006. [5]

All 60 cases of PCOS patient which form the study group belongs to age 15-50 years. We found that HOMA IR increases with the advancing age indicating that the insulin resistance increases with age, but the value is statistically insignificant. Similarly, Joseph L et al [6] also found that insulin resistance increases with age. A S Ryan [7] stated that mechanism of insulin resistance is multifactorial. Ageing is associated with increase weight and fat mass (visceral adiposity) that may cause insulin resistance. They have found that life style modification including weight loss and physical activity cause increase in insulin sensitivity. According to Mohamed et al 2006, [8] the insulin resistance is likely to be a remarkable feature of the physiological aging changes of the human body. It is hence an inevitable risk factor to develop glucose intolerance and other metabolic dysfunction and consequent health hazards. Secretion and clearance of insulin along with its interaction at the target tissues are deranged in the geriatric population.

In the study group, we found that HOMA IR increases as the BMI increases, which is statistically significant (p value < 0.05). Keilah E. Martinez reported in 2017 [9] that as BMI increased, HOMA-IR increased significantly, and within each BMI category, higher levels of body fat were associated with higher levels of HOMA-IR. High BMI were strongly related to insulin resistance. Insulin resistance appears to increase incrementally according to BMI levels primarily and body fat levels secondarily. Including a precise measure of body fat with BMI adds little to the utility of BMI in the prediction of insulin resistance. Similar findings were reported by Tong Y et al. [10] According to study done by Jayshree et al [11] HOMA-IR and fasting insulin values showed a significant positive correlation with BMI. They further stated that both obese and lean women with PCOS are vulnerable to the problems of insulin resistance irrespective of BMI and insulin resistance shows a positive correlation with BMI. Similarly, other authors also [12] noted a close association between HOMA IR and BMI in PCOS patient.

In our study, value of HOMA IR is more in Urban (1.64±0.5) than rural population (1.55±0.6), which is statistically significant (p value < 0.05). According to Mohan et al [13] HOMA-IR levels were higher for residents of urban areas compared to non-urban. A study by C S Yaznik [14] Adiposity, waist circumference, HOMA-IR, insulinogenic index and both fasting and postprandial glucose concentrations increased progressively from rural through to urban slum and urban middle-class men. [14]

In the study done by Bala ji S[15] study rural participants diagnosed with PCOS had raised serum insulin levels in 40% when compared to urban participants which were 44%. Insulin resistance and hyperinsulinemia are considered risk factors for development of atherosclerosis and impaired glucose tolerance. Acanthosis nigricans is considered as an important cutaneous marker of hyperinsulinemia

This study correlates with Bharathi et al[4] showed that the prevalence of PCOS diagnosed by the Rotterdam criteria in community-dwelling women from rural and urban areas of Chennai was 6 per cent.

## CONCLUSION

Insulin resistance is common abnormality in PCOS, but it is not the universal feature. HOMA IR allow identification of insulin resistance. The test is easy to perform and cost effective. It allows identification of insulin resistance in PCOS women allowing improved approaches in management of therapeutic target in these women. This will be of utmost importance in future, as epidemic of diabetes and cardiovascular disease affect the women worldwide.

Work Attributed to: Biochemistry and Obstericts & Gynaecology department of Darbhanga Medical College and Hospital, Laheriasarai, Bihar, India

**Author's Contribution:**

***Dr. Amrita-*** Definition of intellectual content, Literature survey, Prepared first draft of manuscript, implementation of study protocol, data collection, data analysis and preparation of Figures

***Dr. Prahlad Prasad Gupta-*** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision;

***Dr. Kundan Amitav-*** manuscript preparation and submission of article, Coordination and Manuscript revision, Design of study, statistical Analysis and Interpretation;

***Dr. Sude Kumar Singh-*** Review Manuscript; Literature survey

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## REFERENCES

1. Rosenfield RL, Ehrmann DA. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocr Rev. 2016 Oct;37(5):467-520. doi: 10.1210/er.2015-1104. Epub 2016 Jul 26. PMID: 27459230; PMCID: PMC5045492.
2. Shirazi FKH, Khodamoradi Z, Jeddi M. Insulin resistance and high molecular weight adiponectin in obese and non-obese patients with Polycystic Ovarian Syndrome (PCOS). BMC Endocr Disord. 2021 Mar 9;21(1):45. doi: 10.1186/s12902-021-00710-z. PMID: 33750349; PMCID: PMC7941970.
3. Otto-Buczkowska E, Grzyb K, Jainta N. Polycystic ovary syndrome (PCOS) and the accompanying disorders of glucose homeostasis among girls at the time of puberty. Pediatr Endocrinol Diabetes Metab. 2018;24(1):40-44. doi: 10.18544/PEDM-24.01.0101. PMID: 30083660.
4. Bharathi V, Swetha S, Neerajaa J, Madhavica V, Janani D, Rekha S, Ramya S., Usha B. An epidemiological survey: Effect of predisposing factors for PCOS in Indian urban and rural population. Middle East Fertility Society Journal. 2017;22(4):313-316. https://doi.org/10.1016/j.mefs.2017.05.007. (https://www.sciencedirect.com/science/article/pii/S1110569016301510)
5. Kshetrimayum C, Sharma A, Mishra VV, Kumar S. Polycystic ovarian syndrome: Environmental/occupational, lifestyle factors; an overview. J Turk Ger Gynecol Assoc. 2019 Nov 28;20(4):255-263. doi: 10.4274/jtgga.galenos.2019.2018.0142. Epub 2019 Mar 1. PMID: 30821135; PMCID: PMC6883751.
6. Evans JL, Goldfine ID. Aging and insulin resistance: just say iNOS. Diabetes. 2013 Feb;62(2):346-8. doi: 10.2337/db12-1239. PMID: 23349542; PMCID: PMC3554381.
7. Gordon BA, Benson AC, Bird SR, Fraser SF. Resistance training improves metabolic health in type 2 diabetes: a systematic review. Diabetes Res Clin Pract. 2009 Feb;83(2):157-75. doi: 10.1016/j.diabres.2008.11.024. Epub 2009 Jan 9. PMID: 19135754.
8. Al-Beltagi M, Bediwy AS, Saeed NK. Insulin-resistance in paediatric age: Its magnitude and implications. World J Diabetes. 2022 Apr 15;13(4):282-307. doi: 10.4239/wjd.v13.i4.282. PMID: 35582667; PMCID: PMC9052009.
9. Martinez KE, Tucker LA, Bailey BW, LeCheminant JD. Expanded Normal Weight Obesity and Insulin Resistance in US Adults of the National Health and Nutrition Examination Survey. J Diabetes Res. 2017; 2017:9502643. doi: 10.1155/2017/9502643. Epub 2017 Jul 25. PMID: 28812029; PMCID: PMC5547730.

10. Tong Y, Xu S, Huang L, Chen C. Obesity and insulin resistance: Pathophysiology and treatment. Drug Discov Today. 2022 Mar;27(3):822-830. doi: 10.1016/j.drudis.2021.11.001. Epub 2021 Nov 9. PMID: 34767960.

11. Jayashree S, Shylaja P, Ajjammanavar V. Insulin resistance in obese and lean women with polycystic ovarian syndrome. Int J Reprod Contracept Obstet Gynecol 2019; 8:63-8. DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20185150

12. Calcaterra V, Verduci E, Cena H, Magenes VC, Todisco CF, Tenuta E, Gregorio C, De Giuseppe R, Bosetti A, Di Profio E, Zuccotti G. Polycystic Ovary Syndrome in Insulin-Resistant Adolescents with Obesity: The Role of Nutrition Therapy and Food Supplements as a Strategy to Protect Fertility. Nutrients. 2021 May 28;13(6):1848. doi: 10.3390/nu13061848. PMID: 34071499; PMCID: PMC8228678.

13. Thanikachalam M, Fuller CH, Lane KJ, Sunderarajan J, Harivanzan V, Brugge D, Thanikachalam S. Urban environment as an independent predictor of insulin resistance in a South Asian population. Int J Health Geogr. 2019 Feb 12;18(1):51-58. doi: 10.1186/s12942-019-0169-9. PMID: 30755210; PMCID: PMC6373002.

14. Yajnik CS, Katre PA, Joshi SM, Kumaran K, Bhat DS, Lubree HG, Memane N, Kinare AS, Pandit AN, Bhave SA, Bavdekar A, Fall CH. Higher glucose, insulin and insulin resistance (HOMA-IR) in childhood predict adverse cardiovascular risk in early adulthood: the Pune Children's Study. Diabetologia. 2015 Jul;58(7):1626-36. doi: 10.1007/s00125-015-3602-z. Epub 2015 May 5. PMID: 25940643; PMCID: PMC4472941.

15. Balaji S, Amadi C, Prasad S, Bala Kasav J, Upadhyay V, Singh AK, Surapaneni KM, Joshi A. Urban rural comparisons of polycystic ovary syndrome burden among adolescent girls in a hospital setting in India. Biomed Res Int. 2015;12:158951. doi: 10.1155/2015/158951. Epub 2015 Jan 5. PMID: 25629036; PMCID: PMC4299689.