Original Research

Assessing The Correlation Of Fasting Plasma Insulin Resistance And Levels To Ovarian Volume Using Hemostasis Model Assessment 2 In Females With Polycystic Ovaries

Dr. Hardika Poonia[1], Dr. Harshita Srivastava[2], Dr. D.S.S.K Raju[3]

[1]PG resident, Department of Obstetrics & Gynaecology,JNU Hospital, Jaipur, Rajasthan
[2]Assistant Professor, Department of Obstetrics & Gynaecology, Dr. SoneLal Patel Autonomous State Medical College, Pratapgarh, Uttar Pradesh
[3]Associate Professor, Department of Biochemistry, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram, Andhra Pradesh

Corresponding author
Dr. D.S.S.K Raju
Associate Professor, Department of Biochemistry, Maharajah's Institute of Medical Sciences, Nellimarla, Vizianagaram, Andhra Pradesh
Email id: dsskraju@gmail.com

Abstract
Background: PCOS (polycystic ovarian syndrome) is a disease affected by lifestyle and its incidence has been increasing globally including in India warranting its exploration.
Aim: The present study aimed to assess the increase in insulin resistance with increasing size of the ovary by using a HOMA 2 model. The study assessed the correlation of fasting plasma insulin resistance and levels to ovarian volume using hemostasis model assessment 2 (HOMA 2) in females with polycystic ovaries.
Methods: The study assessed 108 females who had PCOS and were assessed for ovarian volume utilizing transabdominal sonography. For all the subjects, blood samples were collected under strict aseptic and sterile conditions and were sent for assessment of fasting blood sugar and fasting plasma insulin levels. The HOMA 2 calculator was used to assess beta cell function, insulin sensitivity, and insulin resistance. Data gathered were statistically analyzed.
Results: The mean BMI and age of the study subjects were 25.55kg/m2 and 26.1 years. Hoarseness of voice, male pattern pubic hair, clitoromegaly, acanthosis, acne, hirsutism, and alopecia were seen in 1.85%, 48.15%, 75.92%, 12.96%, 59.26%, 72%, and 79.6% study subjects respectively. A significant positive correlation was seen in fasting plasma insulin and BMI levels with p=0.02, insulin resistance and BMI with p=0.02, fasting plasma insulin and total ovarian volume with p=0.003, and insulin resistance with p=0.004. Also, a positive correlation was noted in insulin resistance and volume of large ovaries and a negative correlation in insulin sensitivity and ovarian volume.
Conclusions: The present study concludes that an increase in the volume of the ovary can be taken as an indicator of an increase in insulin resistance in females with PCOS.
Keywords: insulin resistance, insulin sensitivity, PCOS, Polycystic ovary syndrome, obesity

Introduction
PCOS (polycystic ovarian syndrome) is a disease governed and affected by lifestyle and affects a large number of females globally including in India. In developing nations such as India, an increase in the incidence of PCOS has been attributed to lifestyle changes, stress, modernization, and westernization. The increase in prevalence is also increasing with the global increase in the incidence of Type 2 diabetes mellitus.[1]

Michael L Leventhal and Irwing F Stein in the year 1935 were the first ones to describe a symptom complex associated with anovulation. They explained seven subjects had enlarged polycystic ovaries, hirsutism, and amenorrhea. Authors further reported that all subjects had regular menstrual cycles and two of the females conceived after bilateral ovarian wedge resection involving removal of ½ to 3/4th of each ovary.PCOS is one of the most common conditions affecting females from the reproductive age group and affects nearly 8-13% of females and nearly 70% of the

females with PCOS remain undiagnosed. The rates of PCOS are high in Indian subjects in comparison to Caucasian subjects.[2]

Based on the geographical region, one out of every 5 females from the reproductive age group and 2 of every 5 adolescent females are diagnosed with PCOS. There is an estimated prevalence of nearly 225 females in the Indian context. Also, an increasing trend is seen in urban females compared to females residing in rural areas. Also, the disease has a high prevalence in high socioeconomic groups owing to a higher prevalence of insulin resistance, overweight, and obesity with adaptation to a more sedentary lifestyle, labor-saving devices, and access to high-calorie foods. Various literature studies have reported contradictory results with no link between PCOS and obesity confirming a higher genetic component.[3]

Insulin resistance is commonly seen in obese subjects and less in lean females with PCOS. Overall prevalence is in the range of 50% to 75% females. Insulin sensitivity is reduced by a mean of 35-40% in females with PCOS compared to females with non-insulin-dependent diabetes mellitus. Nearly 35% of females with PCOS have impaired glucose tolerance and 7-10% have diabetes mellitus. On the contrary, females with type 2 diabetes mellitus are at 6 times higher risk of PCOS compared to non-diabetic females of similar age. However, presently, no clinical test exists for the detection of insulin resistance in general subjects apart from OGTT (oral glucose tolerance test).[4] The present study aimed to assess the correlation of fasting plasma insulin levels and ovarian volume, and insulin resistance using HOMA 2 (homeostasis model assessment 2) in females with polycystic ovaries.

Materials and methods
The present cross-sectional clinical study aimed to assess the correlation of fasting plasma insulin levels and ovarian volume, and insulin resistance using HOMA 2 (homeostasis model assessment 2) in females with polycystic ovaries. The study was done at the Outpatient Department of Obstetrics & Gynaecologyof the Institute. Verbal and written informed consent were taken from all the subjects before study participation.

The study assessed 108 subjects who visited the institute within the defined study period. The inclusion criteria for the study were nulliparous females aged 18 to 35 years, with the diagnosis of polycystic ovaries using Rotterdam criteria, who were willing to participate in the study. The exclusion criteria were subjects on metformin during the study period, previously diagnosed PCOS women who have already undergone surgery on ovaries, and subjects who did not give consent for study participation.

After the final inclusion of the study subjects, a detailed history was recorded for all the subjects followed by a comprehensive clinical examination focusing primarily on menstrual history and clinical features of hyperandrogenism. Subjects were then sent for transabdominal ultrasonography to assess the ovarian volume. Ovarian volume was estimated as LxBxH/2. Ovarian volume measurement was done by a single examiner expert in the field. A single sample from venous blood was collected and sent to assess fasting blood sugar levels and fasting plasma insulin levels. Data was collected in a preformed structured proforma.

Data gathered was entered in MS Excel format to assess insulin resistance. Parameters assessed were BMI, age, beta cell function, insulin resistance, insulin sensitivity, male pattern pubic hair, clitoromegaly, acne, alopecia, hirsutism, and ovarian volume. To evaluate insulin resistance, the HOMA2 calculator was used which gives insulin sensitivity, beta cell function, and insulin resistance for a given plasma insulin and fasting blood sugar values.

Results
The present cross-sectional clinical study aimed to assess the correlation of fasting plasma insulin levels and ovarian volume, and insulin resistance using HOMA 2 (homeostasis model assessment 2) in females with polycystic ovaries. The study assessed 108 females who had PCOS and were assessed for ovarian volume utilizing transabdominal sonography. For all the subjects, blood samples were collected under strict aseptic and sterile conditions and were sent for assessment of fasting blood sugar and fasting plasma insulin levels. Among 108 females included, the majority were in the age range of 21-25 years and the mean age of the study subjects was 26.1 years.

It was seen that in 83% of females, BMI was high with 58 obese females and 32 overweight females in the study. The mean BMI of study subjects was 25.55 kg/m2. The majority of the females only reported mild menstrual cycle disturbance reported in 89% of females. The most common physical feature was alopecia seen in 80% of females followed by clitoromegaly in 75% of females. Other features were acanthosis, male pattern pubic hair, hirsutism, and acne in 13%, 48%, 72%, and 59% of females respectively.

The study results showed that concerning the quantitative values, a significant positive correlation was seen in plasma insulin level and BMI of study subjects with a p-value of 0.02. Also, a significant positive correlation was seen in BMI and insulin resistance with p=0.02. The study results also showed a significant positive correlation between total ovarian volume and fasting plasma insulin level with p=0.003 (Table 1).

It was also reported that a positive correlation was seen between insulin resistance and ovarian volume with p=0.004. A positive correlation was seen between beta cell function and BMI. However, the difference was statistically non-significant. Similarly, the relationship between insulin resistance and the volume of the large ovary was positive and non-

significant. Also, a positive correlation was seen between beta cell function and total ovarian volume. On the contrary, a negative correlation was seen in insulin sensitivity, to the volume of the large ovary and total ovarian volume (Table 2).

Table 1: Correlation of BMI to other parameters in study subjects

S. No	Parameters	Pearson correlation	p-value
1.	Insulin resistance	0.300	**0.02**
2.	Insulin sensitivity	-.258	0.06
3.	Beta cell function (%)	.132	0.333
4.	The volume of the large ovary	.0.32	0.805
5.	Total ovarian volume	.116	0.394
6.	Fasting plasma insulin	0.306	**0.02**

Table 2: Correlation in total ovarian volume and other parameters in study subjects

S. No	Parameters	Pearson correlation	p-value
1.	Insulin resistance	0.385	**0.004**
2.	Insulin sensitivity	-.174	0.201
3.	Beta cell function (%)	.218	0.112
4.	Fasting plasma insulin	.395	**0.003**
5.	BMI	.116	0.394

Discussion

The present study assessed 108 females who had PCOS and were assessed for ovarian volume utilizing transabdominal sonography. For all the subjects, blood samples were collected under strict aseptic and sterile conditions and were sent for assessment of fasting blood sugar and fasting plasma insulin levels. Among 108 females included, the majority were in the age range of 21-25 years and the mean age of the study subjects was 26.1 years. These data were comparable to the previous studies of Reid SP et al[5] in 2017 and Keen M et al[6] in 2017 where authors assessed subjects with PCOS, demographics, and disease data comparable to the present study in their respective studies.

The study results showed that in 83% of females, BMI was high with 58 obese females and 32 overweight females in the study. The mean BMI of study subjects was 25.55 kg/m2. The majority of the females only reported mild menstrual cycle disturbance reported in 89% of females. The most common physical feature was alopecia seen in 80% of females followed by clitoromegaly in 75% of females. Other features were acanthosis, male pattern pubic hair, hirsutism, and acne in 13%, 48%, 72%, and 59% of females respectively. These results were consistent with the findings of Gracelyn L et al[7] in 2015 and Singh A et al[8] in 2018 where clinical features of PCOS reported by the authors in their studies were comparable to the results of the present study.

It was seen that concerning the quantitative values, a significant positive correlation was seen in plasma insulin level and BMI of study subjects with a p-value of 0.02. Also, a significant positive correlation was seen in BMI and insulin resistance with p=0.02. The study results also showed a significant positive correlation between total ovarian volume and fasting plasma insulin level with p=0.003. These findings were in agreement with the results of Sowmya D et al[9] in 2017 and Choudhary A et al[10] in 2017 where a significant positive correlation was seen in plasma insulin level and BMI similar to the present study as reported by the authors.

The study results also showed that a positive correlation was seen between insulin resistance and ovarian volume with p=0.004. A positive correlation was seen between beta cell function and BMI. However, the difference was statistically non-significant. Similarly, the relationship between insulin resistance and the volume of the large ovary was positive and non-significant. Also, a positive correlation was seen between beta cell function and total ovarian volume. On the contrary, a negative correlation was seen in insulin sensitivity, to the volume of the large ovary and total ovarian volume. These results were in line with the findings of Malik S et al[11] in 2014 and Balaji S et al[12] in 2015 where a positive correlation in insulin resistance and ovarian volume and a positive correlation in beta cell function and BMI was also reported by the authors as in the present study.

Conclusions

The present study, within its limitations, concludes that an increase in the volume of the ovary can be taken as an indicator of an increase in insulin resistance in females with PCOS. However, further longitudinal studies in the future will be needed to reach a definitive conclusion.

References

1. Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of Polycystic Ovarian Syndrome in Indian Adolescents. J Pediatr Adolesc Gynecol. 2011;24:223-27.
2. Azziz R, Dumesic DA, Goodarzi MO. Polycystic ovary syndrome: an ancient disorder. Fertil Steril. 2011; 95:1544-48.

3. Joshi B, Mukherjee S, Patil A, Purandare A, Chauhan S, Vaidya R. A cross-sectional study of polycystic ovarian syndrome among adolescent and young girls in Mumbai, India. Indian J. Endocrinol. Metab. 2014;18:317-24.

4. Azziz R, Marin C, Hoq L, Badamgarav E, Song P. Health Care-Related Economic Burden of the Polycystic Ovary Syndrome during the Reproductive Life Span. J Clin Endocrinol Metab. 2005;90:4650-58.

5. Reid SP, Kao CN, Pasch L, Shinkai K, Cedars MI, Huddleston HG. Ovarian morphology is associated with insulin resistance in women with polycystic ovary syndrome: a cross-sectional study. Fertil Res Pract. 2017;3:1-7.

6. Keen M, Shah I, Sheikh G. Cutaneous manifestations of polycystic ovary syndrome: A cross-sectional clinical study. Indian Dermatol Online J. 2017;8:104.

7. Gracelyn L, Pushpagiri N. Prevalence of glucose tolerance test abnormalities in women with polycystic ovarian syndrome. Int J Reprod Contraception Obstet Gynecol. 2015;4:1739 - 45.

8. Singh A, Vijaya K, Sai Laxmi K. Prevalence of polycystic ovarian syndrome among adolescent girls: a prospective study. Int J Reprod Contraception Obstet Gynecol. 2018;7:4375.

9. Sowmya D, Anitha S. Clinical study of the polycystic ovarian syndrome (PCOS) in the tertiary care center. Int J Reprod Contraception Obstet Gynecol. 2017;6:3247.

10. Choudhary A, Jain S, Chaudhari P. Prevalence and symptomatology of polycystic ovarian syndrome in Indian women: is there a rising incidence? Int J Reprod Contraception Obstet Gynecol. 2017;6:4971.

11. Malik S, Jain K, Talwar P, Prasad S, Dhorepatil B, Devi G, et al. Management of Polycystic Ovary Syndrome in India. Fertil Sci Res. 2014;1:23-43.

12. Balaji S, Amadi C, Prasad S, Kasav JB, Upadhyay V, Singh AK, et al. Urban-Rural Comparisons ofPolycystic Ovary Syndrome Burden among Adolescent Girls in a Hospital Setting in India. Biomed Res Int. 2015;2015:1-10.