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Research Article

Association between Insulin Resistance and Abnormal Menstrual Cycle in Females with Polycystic Ovary Syndrome

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ABSTRACT
Aim: To determine the association between insulin resistance and abnormal menstrual cycle in females with polycystic ovary syndrome.
Materials and methods: The prospective observational study was conducted in the Department of Gynaecology and Obstetrics. Total 100 females had complaints of abnormal menstruation, acne, hirsutism, and problems with fertility, and 100 controls having long-standing history of normal menstrual cycles, were enrolled for the study. Demographic, menstrual, clinical, and family history data were collected using a structured questionnaire. Anthropometric measurements and transvaginal ultrasonography were performed. Fasting blood samples were analyzed for glucose, lipid profile, insulin, FSH, LH, and testosterone using standard methods. HOMA-IR >2.5 was considered indicative of insulin resistance.
Results: The mean age was comparable between groups ($p = 0.455$), while BMI and WHR were significantly higher in women with PCOS. PCOS women also had significantly higher fasting glucose, insulin, HOMA-IR, total cholesterol, LDL, triglycerides, LH/FSH ratio, and testosterone levels than controls. Among PCOS subgroups, fasting insulin, HOMA-IR, LH/FSH ratio, and testosterone increased significantly with longer menstrual cycle intervals ($p < 0.05$), indicating greater insulin resistance and hyperandrogenism with increasing menstrual irregularity.
Conclusion: Oligomenorrhea (>45-day cycles) was common in women with PCOS, with increasing menstrual irregularity associated with greater hyperandrogenism and insulin resistance. Menstrual cycle length may serve as a simple clinical predictor of insulin resistance in PCOS.

Keywords: Insulin Resistance, Abnormal Menstrual Cycle, Polycystic Ovary Syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common reproductive endocrine disorder in women of reproductive age today.[1] Studies have shown that its current prevalence is 5.5%-16.0%.[2] PCOS is characterized by polycystic ovaries, oligomenorrhea or amenorrhea, hyperandrogenemia, insulin resistance (IR), weight gain and infertility. It can lead to various health problems, such as cardiovascular disease, diabetes and hypertension.[3]

The cause of PCOS is not clearly stated, but many signs show a strong link between the metabolic and endocrine system. Clinical manifestations of menstrual cycle disorders include oligomenorrhea and amenorrhea. Some studies have shown that about 30% of patients with PCOS exhibit normal menstruation, 85%-90% of women with scanty menstruation have PCOS, and 30%-40% of women with amenorrhea have PCOS. The current diagnostic criterion for amenorrhea in patients with PCOS is a period of menolipsis for more than three months, but many patients with amenorrhea did not pay attention to this symptom and were not timely diagnosed and treated. Additionally, miscarriages and adverse pregnancy outcomes are usually seen in patients with PCOS, particularly in those with amenorrhea.[4] Therefore, early diagnosis and intervention for amenorrhea in patients with PCOS are essential.

IR and menstrual cycle disorders are characteristics of PCOS. When a woman's hormone levels are affected, this in turn disrupts ovarian function, which lead to menstrual complications such as anovulation and amenorrhea.[5] Currently, in addition to menstrual cycle disorders, IR in patients with PCOS has a significant impact on the health of women of childbearing age, which is measured by the homeostasis model assessment: insulin resistance (HOMA-IR) index.[6] As sex hormone secretion influences the menstrual cycle, IR interacts with the patient's body estrogen levels, higher estrogen levels can increase

luteinizing hormone (LH) secretion and decrease follicle stimulating hormone (FSH) secretion, which in turn leads to follicular membrane cell and granulosa cell hyperplasia. In patients with PCOS, insulin increases the sensitivity of the adrenal cortex to the activationof adrenocorticotropic hormones, which further increases androgen secretion and consequent disruption of the menstrual cycle.[6] IR is a key characteristic of PCOS and is associated with worsening of other PCOS features, it increases the risk of infertility and cardiovascular disease in the patients with PCOS. As for abnormal menstrual cycles, a study published in 1993 reported that it is significantly associated with IR.[7] From then, some studies have studied this association between IR and the menstrual cycle in PCOS.[8] However, there were some limitations of the study design in these studies, or they did not well control the important counfounders/biases to assess the association between these two indexes in PCOS.

Therefore, we designed a study to determine the association between insulin resistance and abnormal menstrual cycle in females with polycystic ovary syndrome.

MATERIALS AND METHODS

After obtaining clearance from institutional ethical committee, this prospective observational study was conducted in the Department of Gynaecology and Obstetrics. Total 100 females had complaints of abnormal menstruation, acne, hirsutism, and problems with fertility, and 100 controls having long-standing history of normal menstrual cycles, were enrolled for the study.

Diagnostic Criteria

Using the Rotterdam 2003 criteria, PCOS cases were diagnosed when two of these three conditions were present: 1) oligo- or anovulation, 2) biochemical and/or clinical markers of hyperandro genism, and 3) evidence of polycystic ovarian morphology on ultrasonographic examination.

A measurement of 12 or more 2–9 mm-cysts in one or both ovaries and/or a volume above 10 ml of either ovary was used to diagnose polycystic ovarian morphology (Rotterdam Diagnostic Criteria, 2004). Controls were diagnosed if they had a long-standing history of normal menstrual cycles, had no evidence of hirsutism [modified Ferriman-Gallwey (mFG) score 3] or polycystic ovarian morphology, as determined by ultrasonography.

Participants in the PCOS cohort were grouped into three sets based on the time between episodes of vaginal bleeding: <45 days, 45–90 days, and more than 90 days.

Inclusion Criteria

- Women meeting the established diagnostic criteria for PCOS.
- Participants with complete information regarding menstrual cycle length and relevant hormonal medication history.

Exclusion Criteria

- Thyroid dysfunction, based on abnormal TSH levels.
- Hyperprolactinemia, based on elevated prolactin levels.
- 21-hydroxylase-deficient non-classic adrenal hyperplasia, based on 17-hydroxyprogesterone levels.
- Clinically suspected Cushing's syndrome or androgen-secreting neoplasms.
- Pregnancy at the time of study or within the previous year.
- Use of oral contraceptives or other medications affecting the hypothalamic–pituitary–ovarian axis within the previous 6 months.
- Major systemic diseases, including autoimmune disease, malignancy, or central nervous system disorders.
- Previous treatment with chemotherapy or immunosuppressive agents.
- Incomplete or missing menstrual cycle information.
- Use of hormonal medication within the previous 3 months.

Acquisition of Parameters

Demographic and medical history data were collected by having all participants fill out a questionnaire. Data included personal information, relevant family history, menstrual history, skin conditions linked to hyperandrogenism (hirsutism, acne), and metabolic disease. A complete medical evaluation was carried out on each subject including taking height, weight, waist and hip dimension, and conducting a transvaginal pelvic ultrasound for antral follicle counting. Fasting base line blood samples were drawn to measure biochemical and hormonal parameters at the follicular or preovulatory stage of the menstrual cycle (days2–4) or randomly for subjects with no menstrual bleeding. Subjects were instructed to abstain from everything but water for at least 8h prior to sampling. Glucose

and lipid markers including total cholesterol (TC), triglycerides (TGs), low-density lipoprotein (LDL), and high-densitylipoprotein (HDL) were assessed Insulin levels were determined by sandwich chemiluminescent immunoassay (CLIA). HOMA IR value above 2.5 was used to indicate IR. The follicle stimulating hormone (FSH), luteinizing hormone (LH), and testosterone were measured using CLIA.

Statistical Analysis

Descriptive statistics were expressed as mean ± standard error (SE). Mean values between groups were compared using one-way analysis of variance (ANOVA). Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. Stepwise multiple linear regression analysis was performed to compare mean HOMA-IR values among controls and different menstrual cycle-length groups, while adjusting for age and BMI. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The mean age was comparable between the control and PCOS groups, with no statistically significant difference (26.7 ± 6.5 vs 27.5 ± 6.0 years; p = 0.455). However, women with PCOS had significantly higher BMI and WHR (p < 0.05). Metabolic parameters, including fasting glucose, fasting insulin, and HOMA-IR, were significantly elevated in the PCOS group, indicating greater insulin resistance. The PCOS group also showed significantly higher total cholesterol, LDL, triglycerides, LH/FSH ratio, and testosterone levels compared with controls. HDL levels were also statistically different between groups (Table 1).

The three menstrual cycle groups were comparable in terms of age, BMI, WHR, fasting glucose, and lipid profile, with no statistically significant differences (p > 0.05). However, fasting insulin and HOMA-IR increased progressively with longer menstrual cycles, reaching statistical significance (p < 0.05), suggesting greater insulin resistance in women with cycles >90 days. Similarly, LH/FSH ratio and testosterone levels increased with increasing cycle length (p < 0.05), indicating greater hormonal disturbances with prolonged menstrual cycles. Overall, longer menstrual cycle duration was associated with higher insulin resistance and increased androgenic abnormalities, while anthropometric and lipid parameters remained comparable across groups (Table 2).

Table 1: Characteristics of controls and PCOS women

Variable	Control Group (N=100)	PCOS Group (N=100)	p-value
Age (years)	26.7 ± 6.5	27.5 ± 6.0	0.455
BMI (kg/m²)	23.7 ± 2.3	28.6 ± 1.9	<0.001
Waist- Hip ratio	0.80 ± 0.20	0.84 ± 0.11	0.041
Fasting glucose (mmol/L)	4.53 ± 0.6	5.76 ± 0.6	<0.001
Fasting insulin (µIU/mL)	7.2 ± 2.3	9.01 ± 3.5	<0.001
HOMA-IR	1.48 ± 1.02	2.29 ± 2.87	0.006
Total cholesterol (mmol/L)	4.60 ± 1.1	4.99 ± 0.89	0.007
HDL (mmol/L)	1.50 ± 0.5	1.65 ± 0.6	0.045
LDL (mmol/L)	2.28 ± 0.73	2.86 ± 0.82	<0.001
Triglycerides (mmol/L)	1.00 ± 0.60	1.48 ± 0.94	<0.001
LH/FSH ratio	0.60 ± 0.51	1.69 ± 1.21	<0.001
Testosterone (nmol/L)	1.4 ± 0.5	2.5 ± 0.7	<0.001

Table 2: Characteristics of PCOS parameters among groups of varying menstrual cycle length

Variable	<45 days (n=21)	45–90 days (n=51)	>90 days (n=28)	p-value
Age (years)	27.8 ± 6.2	27.4 ± 6.0	27.6 ± 5.8	0.457
BMI (kg/m²)	27.71 ± 1.10	27.75 ± 1.72	27.68 ± 1.76	0.936
WHR	0.82 ± 0.11	0.83 ± 0.11	0.84 ± 0.11	0.304

Fasting glucose (mmol/L)	5.19 ± 0.59	5.13 ± 0.54	5.09 ± 0.51	0.157
Fasting insulin (µIU/mL)	8.7 ± 2.9	9.2 ± 3.7	10.9 ± 4.2	<0.05
HOMA-IR	2.01 ± 2.14	2.09 ± 2.43	2.46 ± 2.77	<0.05
Total cholesterol (mmol/L)	4.96 ± 0.95	4.97 ± 1.00	5.03 ± 0.89	0.487
HDL (mmol/L)	1.66 ± 0.56	1.67 ± 0.52	1.64 ± 0.55	0.802
LDL (mmol/L)	2.78 ± 0.82	2.78 ± 0.76	2.93 ± 0.84	0.192
Triglycerides (mmol/L)	1.81 ± 0.81	1.89 ± 1.00	1.92 ± 1.20	0.468
LH/FSH ratio	1.49 ± 1.45	1.68 ± 1.01	2.02 ± 1.30	<0.05
Testosterone (nmol/L)	2.10 ± 0.96	2.34 ± 1.05	2.65 ± 0.97	<0.05

DISCUSSION

In our investigation, we confirmed significantly higher levels of insulin resistance (IR) and androgen levels in women with PCOS compared with women without PCOS. Further analysis based on the interval between menstrual periods showed a significant association between menstrual irregularity and the severity of IR.

More than half of the women with PCOS had menstrual cycle intervals of 45–90 days, while 20.6% had intervals below 45 days and 28.9% had intervals exceeding 90 days. Overall, more than three-quarters of women with PCOS had overtly irregular menstrual cycles (oligomenorrhea). The high prevalence of menstrual irregularities in our cohort, recruited from an endocrine clinic, may reflect a more severe PCOS phenotype, which likely motivated these women to seek medical attention.[9]

An incidence of insulin resistance (IR) of approximately 65% has been reported in normal-weight women with PCOS, increasing to nearly 95% among obese women with PCOS. In our study, women with PCOS had a significantly higher BMI than controls, although their BMI did not meet the criteria for obesity. Hyperandrogenism, IR-induced hyperinsulinemia, and altered intrafollicular paracrine signaling may impair normal follicular development and ovulation.[10] IR may also adversely affect oocyte development and embryo quality, potentially contributing to lower fertilization and implantation rates in women with PCOS.[11] Therefore, identifying clinical indicators for early detection of IR in PCOS may help improve reproductive outcomes. In our study, menstrual cycle abnormalities were significantly associated with the severity of IR, consistent with findings from previous studies.[12]

The positive correlation between the length of the menstrual bleeding interval and HOMA-IR, with longer intervals associated with higher HOMA-IR levels, suggests that the degree of menstrual irregularity may serve as a simple clinical indicator of the severity of metabolic and endocrine disturbances in women with PCOS.[13]

Oligomenorrhea has been associated with hyperandrogenism. In our study, testosterone levels were significantly higher in women with PCOS and increased progressively with longer menstrual cycle intervals. Previous studies have demonstrated a positive association between serum androgen levels and follicle number in women with and without PCOS, while anti-androgen therapy has been shown to reduce the number and size of ovarian cysts in PCOS.[10] Hyperandrogenism may contribute to PCOS by promoting the recruitment of small follicles, thereby impairing normal follicular selection and development.[14] Thus, elevated androgen levels may contribute to menstrual irregularity through disruption of normal follicular growth. In our subgroup analysis, women with hyperandrogenism and menstrual intervals of 45–90 days or >90 days showed greater insulin resistance, suggesting a possible association between hyperandrogenism and worsening IR in PCOS. This finding is consistent with previous evidence linking hyperandrogenism to an increased risk of type 2 diabetes and obesity[15], potentially through hyperinsulinemia-mediated stimulation of androgen production.[16]

Limitations

There were several limitations to this study. First, the relatively small sample size may have affected the statistical power and reliability of the findings. Second, the observational design and reliance on self-reported information may have introduced potential bias. Finally, participants were recruited from a single clinic, which may limit the generalizability of the findings to the broader population of women with PCOS.

CONCLUSION

Our findings demonstrate that oligomenorrhea (menstrual cycles >45 days) is common among women with PCOS. The severity of androgenic dysfunction increased with worsening oligomenorrhea, while insulin resistance showed a positive association with longer menstrual cycle intervals. These findings suggest that menstrual cycle length, as a simple clinical indicator of menstrual irregularity, may serve as a useful predictor of insulin resistance in women with PCOS.

REFERENCES

1. Garzia E, Galiano V, Marfia G, Navone S, Grossi E, Marconi AM. Hyperandrogenism and menstrual imbalance are the best predictors of metformin response in PCOS patients. Reprod Biol Endocrinol. 2022;20(1):6.
2. Hatziagelaki E, Pergialiotis V, Kannenberg JM, Trakakis E, Tsiavou A, Markgraf DF, , et al. Association between biomarkers of Low-grade inflammation and sex hormones in women with polycystic ovary syndrome. Exp Clin Endocrinol Diabetes. 2020;128(11):723–30.
3. Osibogun O, Ogunmoroti O, Michos ED. Polycystic ovary syndrome and cardiometabolic risk: Opportunities for cardiovascular disease prevention. Trends Cardiovasc Med. 2020;30(7):399–404.
4. Yu T, Wu D, Cao Y, Zhai J. Association Between Menstrual Patterns and Adverse Pregnancy Outcomes in Patients With Polycystic Ovary Syndrome. Front Endocrinol (Lausanne). 2021;12:740377
5. Abraham Gnanadass S, Divakar Prabhu Y, Valsala Gopalakrishnan A. Association of metabolic and inflammatory markers with polycystic ovarian syndrome (PCOS): an update. Arch Gynecol Obstet. 2021;303(3):631–43.
6. Abraham Gnanadass S, Divakar Prabhu Y, Valsala Gopalakrishnan A. Association of metabolic and inflammatory markers with polycystic ovarian syndrome (PCOS): an update. Arch Gynecol Obstet. 2021;303(3):631–43.
7. Robinson S, Kiddy D, Gelding SV, Willis D, Niththyananthan R, Bush A, et al. The relationship of insulin insensitivity to menstrual pattern in women with hyperandrogenism and polycystic ovaries. Clin Endocrinol. 1993;39(3):351–5.
8. Ezeh U, Ezeh C, Pisarska MD, Azziz R. Menstrual dysfunction in polycystic ovary syndrome: association with dynamic state insulin resistance rather than hyperandrogenism. Fertil Steril. 2021;115(6):1557–68.
9. Louwers YV, Laven JS. Characteristics of polycystic ovary syndrome throughout life. Therapeutic Advances in Reproductive Health. 2020;14:2633494120911038.
10. Dumesic DA, Damario MA, Session DR, Famuyide A, Lesnick TG, Thornhill AR, et al. Ovarian morphology and serum hormone markers as predictors of ovarian follicle recruitment by gonadotropins for in vitro fertilization. The Journal of Clinical Endocrinology & Metabolism. 2001;86(6):2538-43.
11. Nikbakht R, Mohammadjafari R, Rajabalipour M, Moghadam MT. Evaluation of oocyte quality in Polycystic ovary syndrome patients undergoing ART cycles. Fertility research and practice. 2021;7(1):2.
12. Brower M, Brennan K, Pall M, Azziz R. The severity of menstrual dysfunction as a predictor of insulin resistance in PCOS. The Journal of Clinical Endocrinology & Metabolism. 2013;98(12):E1967-71.
13. Li X, Yang D, Pan P, Azziz R, Yang D, Cheng Y, et al. The degree of menstrual disturbance is associated with the severity of insulin resistance in PCOS. Frontiers in Endocrinology. 2022;13:873726.
14. Jonard S, Dewailly D. The follicular excess in polycystic ovaries, due to intra-ovarian hyperandrogenism, may be the main culprit for the follicular arrest. Human reproduction update. 2004;10(2):107-17.
15. Persson S, Elenis E, Turkmen S, Kramer MS, Yong EL, Poromaa IS. Higher risk of type 2 diabetes in women with hyperandrogenic polycystic ovary syndrome. Fertility and sterility. 2021;116(3):862-71.
16. Garzia E, Galiano V, Marfia G, Navone S, Grossi E, Marconi AM. Hyperandrogenism and menstrual imbalance are the best predictors of metformin response in PCOS patients. Reproductive Biology and Endocrinology. 2022;20(1):6.