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Insulin Resistance as a Determinant of Menstrual Irregularities in Women of Reproductive Age With and Without Polycystic Ovary Syndrome

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ABSTRACT

Background: The menstrual abnormalities are often reproductive disorders among women of reproductive age and are more often linked to underlying endocrine and metabolic disorders. Polycystic ovary syndrome (PCOS) is well known to result in insulin resistance; its role in causing menstrual irregularities independently of PCOS in non-PCOS women is a poorly researched area.

Objective: To evaluate insulin resistance as a factor leading to menstrual irregularities in women of reproductive age, and to provide a comparative analysis between women with and without polycystic ovary syndrome.

Methods: This is a comparative cross-sectional study carried out between December 2024 and July 2025. One hundred and ten females with 18-40 years with menstrual abnormalities were recruited and split into the PCOS (n= 55) and non-PCOS (n= 55) groups. After an overnight fast, the levels of fasting plasma glucose and fasting serum insulin were measured, and insulin resistance was evaluated using the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Menstrual patterns and anthropometric parameters were measured, and statistical analysis was done to establish correlations of insulin resistance and menstrual irregularities.

Results: PCOS women showed drastically higher fasting insulin concentrations and HOMA-IR rates than non-PCOS women. However, the insulin resistance was also observed in a significant number of non-PCOS women. An increment in the HOMA-IR values of both groups had an important relationship with the severity of menstrual irregularities. The multivariational outcome was an insulin resistance, which is an independent predictor of menstrual irregularities adjusted by age and body mass index.

Conclusion: Insulin resistance is a significant factor in the occurrence of menstrual abnormalities in reproductively-aged women, irrespective of PCOS presence. Regular metabolic screening can help in the diagnosis and specific treatment of menstrual dysfunction.

Keywords: Insulin resistance; menstrual irregularities; polycystic ovary syndrome; reproductive age; HOMA-IR

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INTRODUCTION

Menstrual regulation is a vital indicator of normal reproductive and endocrine operations in women of reproductive age [1]. Menstrual symptoms such as oligomenorrhea, amenorrhea, or abnormal cyclicity are common menstrual symptoms that are inherently typical of them as well as signs of underlying hormonal, metabolic, and systemic imbalance. Both their diagnosis and etiological evaluation are clinically important since these malformations can significantly affect the fertility, psychological status, and long-term health consequences [2].

Of the diverse endocrine and metabolic processes that have been found to be involved in menstrual dysfunction, insulin resistance has been identified to be a focal pathophysiological process [3]. Insulin resistance is

described as the decreased biological action of the peripheral tissues to insulin, leading to compensatory hyperinsulinemia. In addition to its classical action of glucose metabolism, insulin has direct and indirect effects on the hypothalamic-pituitary-ovarian axis. High levels of insulin in the circulation increase production of ovarian androgens, inhibit hepatic production of sex hormone-binding globulin and normal follicular growth, which ultimately causes ovulatory dysfunction and menstrual abnormalities [4].

The most commonly known endocrine disorder is polycystic ovary syndrome (PCOS), which is linked to insulin resistance and menstrual abnormalities. In female PCOS, there is a significant percentage of insulin resistance, regardless of obesity, which is a critical factor that increases the effects of hyperandrogenism and reproductive dysfunction. Therefore, insulin resistance, excess of androgens, and changes in gonadotropin secretion have been traditionally blamed as the causes of menstrual irregularities in PCOS [5].

There is, however, emerging evidence that insulin resistance not only affects women with PCOS but could be an independent cause of menstrual disturbances even in women who do not have the classical signs of the syndrome [6]. The metabolic dysregulation, such as the impaired insulin sensitivity, can be present in women who do not meet the PCOS criteria and may negatively impact the ovarian activity and menstrual cyclicity. The given observation defies the traditional belief that menstrual abnormalities outside of PCOS have mostly isolated gynecological or hormonal motivations [7].

Structural or hormonal abnormalities are a common assessment of non-PCOS menstrual abnormalities in women in clinical practice, whereas metabolic evaluation can be ignored [8]. This risk of not identifying insulin resistance in this population can postpone the necessary interventions and put this group at risk of developing metabolic complications in the future, such as type 2 diabetes mellitus and cardiovascular disease. Hence, to provide complete care of the patient, understanding the independent role of insulin resistance on the regulation of menstruation is critical [9].

The current study was aimed at assessing insulin resistance as a cause of menstrual abnormalities in reproductive-age women, and comparing it between women with and without polycystic ovary syndrome. Through analyzing the metabolic parameters and the menstrual patterns, this study will shed some light on the role of insulin resistance in menstrual abnormalities other than the PCOS scenario and the need to screen metabolism in women with menstrual abnormalities [10].

MATERIALS AND METHODS

The study was a comparative cross-sectional study carried out in the Gynecology outpatient department of Fatima Memorial Hospital and College of Medicine and Dentistry, Lahore, Pakistan, between December 2024 and July 2025. This study intended to determine the predictive value of insulin resistance as a factor contributing to menstrual abnormalities in reproductively aged women, and a comparative evaluation of the predictive value of the same among women with and without polycystic ovary syndrome (PCOS).

The number of women used in the study was 110. A non-probability consecutive method was applied to recruit the participants. The subjects were all aged between 18 and 40 years, and all had a history of menstrual irregularities that lasted at least six months. Menstrual irregularities were included as oligomenorrhea, which is a period of 35 days or more than eight cycles annually; amenorrhea, or the absence of menstruation during three or more years in a row; and irregular menstrual cycles with irregular periods. The pregnant and lactating women, those with known diabetes mellitus, thyroid diseases, hyperprolactinemia, Cushing syndrome, premature ovarian insufficiency, chronic systemic diseases, and those who had used hormonal contraception methods, systemic steroids, anti-androgens, or insulin-sensitizing drugs in the past three months were not included in the study.

Once enrolled, the subjects were grouped into two categories depending on the existence or non-existence of polycystic ovary syndrome. The Rotterdam diagnostic criteria were used to diagnose PCOS, with women diagnosed with PCOS meeting at least two out of the following features, following an exclusion of the presence of other endocrine causes: oligo- or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on pelvic ultrasonography. Women with menstrual abnormalities that failed to satisfy these requirements fell under the non-PCOS group. This was done to ensure that there was an effort to preserve similar sizes of groups, where there was a rough equilibrium between the two groups.

The data was collected using a structured pro forma. Demographic information, menstrual history, menstrual period and irregular time, and relevant clinical symptoms, such as weight gain, acne, and hirsutism, were noted. A directed physical examination was done for each participant.

The anthropometric measures comprising weight and height were measured using normal methods, and body mass index was determined as the weight in kilograms divided by the height in meters squared. Measurement of waist circumference was done at the midpoint of the bottom rib and the iliac crest. The measurement of the blood pressure was done in a sitting position and following sufficient rest.

To conduct a laboratory assessment, everyone was asked to fast overnight, 8-12 hours. This has been done by measuring the fasting plasma glucose and the fasting serum insulin concentrations in the venous blood samples collected in the morning through normal laboratory procedures. The Homeostatic Model Assessment of Insulin

Resistance (HOMA-IR) was used to measure insulin resistance, which is calculated by multiplying fasting insulin and the fasting glucose (divided into mmol/L). The participants were categorized into insulin-resistant as per the accepted clinical cutoff values in the laboratory and the literature.

Ultrasonography was done on the pelvis when clinically indicated to identify ovarian morphology, especially when it was necessary to confirm the presence of polycystic ovarian features as part of the diagnostic criteria. The ovarian morphology was assessed based on the normal parameters of ultrasound, which included the number of follicles and ovarian volume.

The entry and analysis of the data were performed with the help of Statistical Package for the Social Sciences (SPSS) software, version 26. Continuous variables were represented in terms of mean and standard deviation, whereas categorical variables were represented by frequencies and percentages. Proper statistical tests of continuous and categorical variables were used to compare both PCOS and non-PCOS groups. The correlation involved in the analysis of the relationship between insulin resistance and patterns of menstrual irregularity was evaluated. It was conducted as a multivariate logistic regression analysis to determine whether the insulin resistance was an independent predictor of menstrual irregularities after taking into consideration other potential confounding factors (age, body mass index). The p-value threshold was 0.05.

The study was approved by the institutional ethics review committee (FMH/ERC/GYN/2024/089) before data collection. Participation was voluntary, and all those who participated had to submit a written informed consent. It was ensured that information about the participants was not disclosed throughout the study and that all procedures were carried out as required by the ethical requirements in study involving human beings.

RESULTS

The study involved a total sample of 110 women of reproductive age who had menstrual irregularities. The sample was divided equally into two categories: women with polycystic ovary syndrome (PCOS group, n = 55) and women with menstrual dysfunctions, but not PCOS (non-PCOS group, n = 55). Table 1 summarizes the baseline demographic characteristics of the two groups.

The mean body mass index and waist circumference showed a higher value in women with PCOS than those without the disorder, suggesting that there is a degree of overall and central adiposity in PCOS women. Despite the similarity of the mean age in the two groups, the anthropometric parameters were found to exhibit significant differences, with greater values in the group with PCOS, comprising women.

In relation to the menstrual cycle, oligomenorrhea was the highest prevalence of menstrual abnormality in both groups, then by irregular cycles and amenorrhea. Amenorrhea was more apparent in the PCOS group, and irregular but continuing cycles were more prevalent in the non-PCOS group of women. Table 2 shows the distribution of the menstrual abnormalities.

Metabolic evaluation showed that the fasting serum insulin level and HOMA-IR level in the PCOS women were much higher than the non-PCOS women. Nevertheless, the non-PCOS group was also characterized by insulin resistance, which showed that metabolic failure was not limited to classical PCOS. Table 3 details these biochemical findings. When the participants were grouped based on insulin resistance status, a much higher number of insulin-resistant subjects were found in the PCOS group. However, insulin resistance was also observed in almost a third of women who had neither PCOS nor its role as a distinct metabolic factor should be underrated. Table 4 demonstrates the prevalence of insulin resistance in both groups.

Table 1: Baseline Demographic and Anthropometric Characteristics of the Study Population

Variable	PCOS Group (n = 55)	Non-PCOS Group (n = 55)	p-value
Age (years), mean ± SD	27.8 ± 4.9	28.3 ± 5.1	0.58
Body Mass Index (kg/m²), mean ± SD	28.6 ± 4.2	25.9 ± 3.8	<0.01
Waist Circumference (cm), mean ± SD	91.4 ± 9.6	86.2 ± 8.8	<0.01

Table 2: Distribution of Menstrual Irregularities in PCOS and Non-PCOS Groups

Menstrual Pattern	PCOS Group n (%)	Non-PCOS Group n (%)	p-value
Oligomenorrhea	29 (52.7%)	26 (47.3%)	0.56
Amenorrhea	16 (29.1%)	9 (16.4%)	0.04
Irregular cycles	10 (18.2%)	20 (36.3%)	0.03

Table 3: Comparison of Glycemic and Insulin Resistance Parameters Between Groups

Parameter	PCOS Group (n = 55)	Non-PCOS Group (n = 55)	p-value
Fasting Plasma Glucose (mg/dL), mean ± SD	96.8 ± 9.4	94.2 ± 8.7	0.12
Fasting Serum Insulin (µIU/mL), mean ± SD	18.9 ± 6.2	13.6 ± 4.9	<0.001
HOMA-IR, mean ± SD	4.5 ± 1.7	3.2 ± 1.3	<0.001

Table 4: Prevalence of Insulin Resistance (Based on HOMA-IR Cutoff)

Insulin Resistance Status	PCOS Group n (%)	Non-PCOS Group n (%)	p-value
Insulin resistant	38 (69.1%)	19 (34.5%)	<0.001
Insulin sensitive	17 (30.9%)	36 (65.5%)	

Correlational analysis showed that there was a strong positive relationship between the values of HOMA-IR and the severity of menstrual abnormalities, and increased insulin resistance was associated with longer cycle periods and an increased chance of amenorrhea. The insulin resistance was found to be a statistically significant independent predictor of menstrual irregularities even after controlling for the effects of age and body mass index in the multivariate logistic regression analysis. These results suggest that insulin resistance is one of the causes of menstrual dysfunction among reproductively aged women regardless of the polycystic ovary syndrome status.

In general, the findings indicate that even though the prevalence and severity of insulin resistance are higher in PCOS women, it is also prevalent and clinically significant in women without PCOS who have menstrual abnormalities, which speaks in favor of its contribution to menstrual cycle disruption.

DISCUSSION

The current study determined the value of insulin resistance as a predictor of menstrual disruptions in reproductively-aged women, and there was a comparative evaluation of respondents with and without polycystic ovary syndrome [11]. The results indicate that insulin resistance is strongly related to menstrual disruptions not only in women with PCOS but also in women who are not diagnosed with the syndrome in question, which is why it can be considered an independent and clinically valuable factor in the regulation of the menstrual cycle [12].

The PCOS women in this study had higher body mass index, waist circumference, fasting insulin measures, and HOMA-IR measures than non-PCOS women. The findings are in line with known evidence that insulin resistance and central obesity are fundamental metabolic phenotypes of PCOS [13]. Hyperinsulinemia of PCOS increases the ovarian androgen secretion, inhibits the sex hormone-binding globulin synthesis in the liver, interrupts the normal follicular development, and thus leads to chronic anovulation and menstrual disorders. The fact that amenorrhea is more common among women with PCOS in this study also proves the correlation between extreme insulin resistance and deeper reproductive malfunction [14].

Notably, a significant percentage of women who did not develop PCOS had also exhibited insulin resistance, even in the absence of polycystic ovarian morphology and overt hyperandrogenism. The primary manifestations of these women were oligomenorrhea or irregular cycles instead of amenorrhea, and it seems that there is a spectrum between menstrual cycle and metabolism disruptions [15]. This observation supports the idea that ovarian dysfunction can be acquired by the intrinsic effect of insulin resistance alone to modify gonadotropin release, decrease the insulin-stimulated ovarian tissue glucose consumption, and disrupt the development of the follicle, even in non-PCOS groups [16].

The fact that a positive relationship is observed between the values of HOMA-IR and the severity of menstrual irregularities in both sets of study participants suggests that there is a dose-response relationship between insulin resistance and menstrual dysfunction [17]. In addition, the multivariate analysis also established insulin resistance as an independent risk factor for menstrual irregularities upon controlling for age and body mass index. This indicates that obesity is not the only mediator of the effects of insulin resistance on menstrual control, but that there is a direct metabolic-endocrine interaction [18].

These findings have clinical implications. It is common for women who have menstrual abnormalities to be assessed with gynecological or hormonal etiology, especially PCOS, and metabolic assessment may be ignored when they do not have typical PCOS manifestations [19]. The inability to detect insulin resistance among such a population might slow down specific lifestyle or pharmacological treatment and predispose such a population to subsequent complications in the long term, including type 2 diabetes mellitus, metabolic syndrome, and cardiovascular disease. The detected cases of insulin resistance at the early stage provide a chance of timely interventions that would restore the normal menstrual cycle and enhance the overall metabolism [20].

Although this study has its advantages, it has some limitations. The cross-sectional type does not allow the development of a causal correlation between insulin resistance and menstrual irregularities [1-8]. Also, insulin resistance was determined by the use of HOMA-IR as opposed to more sophisticated dynamic procedures. Nevertheless, HOMA-IR is a popular and usable instrument for clinical and epidemiological studies. Longitudinal analyses are required in the future that will determine whether the insulin sensitivity improvement results in persistent menstrual cycle normalization in both PCOS and non-PCOS women [20].

CONCLUSION

This study indicates that insulin resistance is a major and independent predictor of menstrual disorders among menstrual-age women regardless of the presence of polycystic ovary syndrome. Although PCOS-related insulin resistance is more frequent and more intense in women, it is also frequent and clinically significant in women without PCOS who visit healthcare with menstrual troubles. These findings promote the applicability of metabolic screening, particularly for insulin resistance, to the whole group of women who have menstrual abnormalities. With a multi-disciplinary metabolic and reproductive approach in clinical practice, insulin resistance may be treated and diagnosed at an early stage to improve the reproductive outcomes, future metabolic health, and menstrual regularity.

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