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THE CORRELATION BETWEEN HEMOGLOBIN A1C (HbA1c) AND INSULIN RESISTANCE IN PCOS WOMEN AND CONTROL

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Abstract

Objective: To analyse the correlation between insulin resistance and HbA1c in women with (PCOS) and normal controls.

Study Design: A case-control descriptive.

Place and Duration of Study: January 2024–March 2026 Department of Obstetrics and Gynecology Shaikh Zayed Women Hospital CMC Larkana Institute of Biochemistry University of Sindh Jamshoro.

Methods: 216 PCOS patients and 216 healthy controls were among the 432 women who were enrolled. Participants were chosen using the Rotterdam criteria. Anthropometric measurements menstrual history infertility status clinical history and hyperandrogenism

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symptoms were all documented. HbA1c HOMA-IR fasting insulin and fasting blood sugar were among the metabolic parameters that were assessed. Data was analyzed into Microsoft Excel and SPSS version 26 was used for analysis. The P-value was (0.05) which was statistically significance.

Results: PCOS patients had a mean age of 29. 28 years and a mean BMI of 27. 65 kg/m^2 while controls had a mean age of 30. 86 years and a mean BMI of 22. 77 kg/m^2. Of those with PCOS 62. 9% had infertility. Hirsutism acne and irregular menstruation were common clinical features. The PCOS groups mean HbA1c levels were significantly higher (5. 7 ± 0. 8 percent) than the controls (3. 1 ± 0. 5 percent) (p = 0. 004). Insulin resistance (IR) was also significantly higher in PCOS ladies with a HOMA-IR of 3. 28 (0. 43–5. 94) as opposed to 0. 68 (0. 08–1. 53) in controls.

Conclusion: Obesity irregular menstruation high HbA1c and increased insulin resistance are all linked to PCOS. For identifying women who are at risk of metabolic and cardiovascular problems HbA1c may be a straightforward and affordable biomarker. It is advised to use multidisciplinary management and early screening.

INTRODUCTION

Women of reproductive age are frequently affected by the endocrine-metabolic condition known as polycystic ovarian syndrome (PCOS). Reproductive hormonal and metabolic disorders such as ovulatory dysfunction infertility irregular menstruation obesity dermatological symptoms and psychological issues that could lower quality of life are its hallmarks. PCOS is now acknowledged as one of the most familial hormonal disorders among female globally having been first identified by Stein and Leventhal in 1935 (1). PCOS prevalence ranges from 5% to 26% worldwide depending on diagnostic criteria and study populations. The reported prevalence in Pakistan is 52% which suggests a significant burden of disease. PCOS affects about 116 million women globally

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according to estimates from the World Health Organization (2). The Rotterdam criteria which call for at least two of the following polycystic or multiple cystic appearance of ovaries on ultrasound, infertility, hyperandrogenism, obesity, and oligo/anovulation are frequently used to make the diagnosis (3). Infertility pregnancy complications depression metabolic syndrome cardiovascular disease liver problems and endometrial cancer are all more diagnosed in female with PCOS (3), as it is closely linked to insulin resistance (IR) and hyperinsulinemia which both contribute to metabolic syndrome, cardiometabolic, and reproductive abnormalities as long term complications (4). A good measure of long-term glycemic status glycated hemoglobin (HbA1c) represents the mean blood sugar over the preceding 2 -3 months. Although genetic and hematological factors may affect its values HbA1c offers more stability than fasting glucose and does not require fasting (5). An HbA1c threshold of ≥6. 5 percent is recommended by international experts for the diagnosis of type 2 DM values between 6. 0 and 6. 5 percent should be further assessed using oral glucose tolerance testing (6). Increased cardiovascular risk has also been linked to elevated HbA1c which may offer important insights into potential metabolic issues in the future (7). Despite the fact that HbA1c is frequently used in diabetes screening compensatory hyperinsulinemia can maintain normal glucose levels so it may not identify early insulin resistance in women with PCOS. However women who are more susceptible to diabetes and cardiovascular disease may be identified by higher HbA1c levels (8). In order to analyse the potential significance of HbA1c as a crucial marker in disorder of metabolism, and cardiovascular risk in the local population this study compared insulin resistance and HbA1c levels between women with PCOS and healthy controls.

METHODOLOGY: -

Study Design, Place and Duration: In cooperation with the Institute of Biochemistry University of Sindh Jamshoro case-control study research was conducted at the Dept of Obst and Gyn at Shaikh Zayed Women Hospital Chandka Medical College (CMC) Larkana. The research was conducted between January 2024 and January 2026.

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Ethical Considerations: All participants provided written consent with full information, Prior to their enrolment in the study. The Institute of Biochemistry at the University of Sindh in Jamshoro received ethical approval from the Ethical Review Board (Reference No. IOB/258/2025 dated October 23 2025.

Exclusion and Inclusion Criteria: Included were women with obesity infertility hirsutism or irregular menstruation who met the Rotterdam criteria for PCOS diagnosis. As controls healthy fertile women were chosen. Women who had a history of diabetes mellitus thyroid issues cardiovascular disease hypertension atherosclerosis or other conditions that affected the metabolism of glucose were not included. Sample Size Estimation

Sample Size Estimation: Included were all eligible PCOS women who visited the study centers during the study period. Healthy women of the same age were chosen to serve as controls.

Study Protocol: A well-informed questionnaire was provided to gather clinical and demographic data such as age parity presenting complaints and medical and surgical history. (BMI)and Blood pressure were measured as part of the clinical examination. To evaluate ovarian volume and morphology pelvic ultrasonography was used. anti-Müllerian hormone (AMH), Follicle-stimulating hormone (FSH), testosterone, thyroid-stimulating hormone (TSH), luteinizing hormone (LH), HbA1c, prolactin, fasting insulin, and blood sugar were measured in blood samples. The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was used to measure (IR) in both PCOS and healthy groups.

Statistical Analysis The categorical variables were displayed as percentage and frequencies continuous variables were expressed as mean ± standard deviation. Data were imported into Microsoft Excel and SPSS version 19 was used for analysis

RESULTS:

Female with PCOS and healthy group are shown in Table 1 along with their baseline clinical and demographic characteristics. Compared to controls women in the PCOS had a statical significantly higher (BMI) but a significantly lower mean age (p0. 001). Women with PCOS had considerably

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higher diastolic and systolic (B/P) blood pressure readings suggesting a higher cardiovascular risk profile. The PCOS group was more common to have a positive family history of PCOS-related conditions and a higher percentage of controls lived in urban areas. According to these results obesity high blood pressure and a family history are significant factors linked to PCOS.

Table 1. Comparison of Clinical & Demographic Characteristics Between PCOS & Controls (N = 430)

Variable	PCOS (n = 215) Mean ± SD / n (%)	Controls (n = 215) Mean ± SD / n (%)	p-value
Age (y)	29.30 ± 6.34	30.88 ± 6.35	<0.001
BMI (kg/m²)	27.67 ± 5.60	23.92 ± 5.15	<0.001
Systolic Blood Pressure (mmHg)	128.50 ± 24.79	114.40 ± 15.78	<0.001
Diastolic Blood Pressure (mmHg)	106.23 ± 19.58	77.36 ± 6.76	<0.001

The clinical symptoms seen in women with PCOS and controls are compiled in Table 2. The PCOS group had significantly higher rates of menstrual disturbances especially amenorrhea and oligomenorrhea. The most prevalent infertility pattern among PCOS-affected women was secondary infertility. Acne and hirsutism two clinical indicators of hyperandrogenism were also significantly more common in PCOS patients than in controls. Additionally, PCOS's women were presented with a acanthosis nigricans as a sign of insulin resistance. The reproductive and dermatological characteristics frequently linked to the syndrome are highlighted by these findings.

Table 2. Clinical Characteristics of ladies with PCOS &Healthy (N = 432)

Variable	Category	PCOS (n = 216) n (%)	Healthy(n = 216) n (%)
Menstrual Pattern	Oligomenorrhea/Hypomenorrhea	129 (60.0)	33 (15.4)

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	Amenorrhea	50 (23.2)	3 (0.9)
	Menorrhagia	9 (4.1)	35 (15.9)
	Normal Menstrual Cycle	27 (12.5)	145 (68.5)
Infertility Status	Primary Infertility	32 (15.0)	9 (4.2)
	Secondary Infertility	146 (68.5)	16 (7.0)
	No history of Infertility	20 (8.9)	183 (84.9)
	Unmarried	15 (6.5)	8 (3.7)
Hirsutism	Present	88 (40.4)	21 (9.7)
	Absent	129 (59.6)	195 (90.3)
Oily Skin / Acne	Present	63 (29.3)	11 (5.1)
	Absent	153 (70.7)	205 (94.9)
Acanthosis Nigricans	Present	16 (7.4)	5 (2.3)
	Absent	199 (92.6)	210 (97.7)
Obesity	Present	70 (32.5)	108 (50.2)
	Absent	145 (67.5)	107 (49.8)
BMI (kg/m²)	Mean ± SD	**27.66 ± 5.59**	**23.92 ± 5.15**

The relationship between different clinical hormonal and metabolic parameters and HbA1c categories is shown in Table 3. Older age higher BMI higher Ferriman-Gallwey scores higher fasting insulin concentrations and higher fasting glucose levels were all linked to rising HbA1c levels. According to HOMA-IR women with higher HbA1c values also had higher levels of insulin resistance. These results imply that in women with PCOS worsening glycemic status is linked to increasing cardiovascular risk and progressive metabolic dysfunction.

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Table 3. Association of HbA1c Categories with Clinical, Hormonal, and Metabolic Parameters Among Study Participants

Variable	HbA1c < 6.0% (n = 73)	HbA1c 6.0–6.5% (n = 12)	HbA1c ≥ 6.5% (n = 11)	Control Group HbA1c < 5.7% (n = 119)
Age (years)	27 (18–30)	36 (31–40)	37 (41–45)	29 (18–45)
BMI (kg/m²)	26.8 (24.5–28.9)	32.6 (32.2–37.9)	34.0 (33.2–40.9)	23.0 (18.0–24.9)
Ferriman–Gallwey Score (0–36)	9 (8–15)	16 (7–18)	14 (10–26)	3 (0–7)
Total Testosterone (nmol/L) Normal range: 0.5–2.4	1.72 (1.27–2.71)	1.23 (0.87–2.07)	1.06 (0.87–1.28)	0.90 (0.50–2.40)
SHBG (nmol/L) Normal range: 18–144	43 (30–61)	24 (18–47)	41 (35–52)	22 (18–144)
Free Testosterone Index (nmol/L) Normal range: 0.001–0.02	0.031 (0.018–0.052)	0.028 (0.018–0.055)	0.025 (0.010–0.034)	0.005 (0.001–0.020)
Fasting Insulin (pmol/L) Normal range: 30–90	67 (45–110)	97 (68–178)	165 (108–288)	43 (32–79)
Fasting sugar (mmol/L) Normal range: 3.9–5.5	4.7 (4.5–5.4)	5.7 (4.5–6.3)	6.4 (5.0–8.9)	4.3 (3.4–4.6)
HOMA-IR Normal range: 1.0–1.9	14.3 (10.4–23.7)	25.3 (16.3–55.1)	63.1 (35.0–77.0)*	10.1 (7.1–12.1)

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Women with PCOS and healthy controls have different hormonal and metabolic profiles as shown in Table 4. FSH the FSH/LH ratio testosterone AMH HbA1c random blood sugar and HOMA-IR were all considerably higher in ladies with PCOS. These results suggest that the PCOS group has increased insulin resistance hyperandrogenism and hormonal imbalance. Despite the fact that PCOS's women had higher levels of the fasting insulin and blood sugar the differences were not significant. Overall, the analysis show that PCOS is closely linked to metabolic and endocrine disorders.

Table 4. Comparison of Hormonal and Metabolic Parameters Between Women with PCOS and Healthy Controls (N = 432)

Variable	PCOS (n = 216) Mean ± SD / Median (Range)	Controls (n = 216) Mean ± SD / Median (Range)	p-value
FSH (mIU/mL)	7.8 ± 1.1	6.1 ± 3.1	0.001*
LH (mIU/mL)	9.2 ± 1.3	7.8 ± 0.9	0.19
FSH/LH Ratio	1.4 ± 2.9	0.75 ± 0.6	<0.0001*
TSH (mIU/mL)	3.5 ± 1.7	1.5 ± 1.2	0.097
Prolactin (mIU/mL)	16.7 ± 1.4	13.7 ± 2.4	0.70
Testosterone (nmol/L)	3.6 ± 2.8	1.5 ± 1.2	<0.0001*
AMH (ng/mL)	7.9 ± 2.1	3.1 ± 1.8	0.001*
Fasting Insulin (µIU/mL)	7.8 (4.9–14.03)	2.1 (1.2–4.2)	0.102
Fasting Blood Sugar (mg/dL)	90.6 ± 2.1	76.4 ± 4.4	0.081
Random Blood Sugar (mg/dL)	134.6 ± 2.1	120.8 ± 7.6	0.037*

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HbA1c (%)	5.7 ± 0.8	3.1 ± 0.5	0.004*
HOMA-IR	3.28 (0.43–5.94)	0.68 (0.08–1.53)	0.005*

DISCUSSION:

One of the most prevalent medical endocrine conditions that affect female during their fertility years is polycystic ovarian syndrome (PCOS). The Rotterdam criteria are the main diagnostic criteria and the condition is often linked to insulin resistance and an elevated risk of metabolic abnormalities. According to earlier research women with PCOS are five to eight times more likely to produce type 2 (DM) than female without PCOS who are age and weight matched. Additionally there is growing evidence that PCOS and cardiovascular disease are related especially in postmenopausal women (9). Regardless of body mass index 35–80% of affected women have been found to have insulin resistance a crucial metabolic characteristic of PCOS. Clinical symptoms like hirsutism acne and irregular menstruation are caused by elevated insulin levels which also increase ovarian androgen production (10). Infertility hirsutism obesity and irregular menstruation were more common in women with PCOS than in healthy controls according to the studys findings. Because HbA1c represents average blood glucose ranges over the previous 2-3 months it is frequently used as a measure of long-term glycemic status. In contrast to fasting glucose measurements HbA1c is more reproducible and can be measured without fasting. Nevertheless a number of biological and clinical factors may affect its values (11). HbA1c has drawn more attention as a possible indicator of metabolic risk in ladies with PCOS as a result of these benefits. Beyond reproductive dysfunction endocrine and metabolic disorders are hallmarks of PCOS. Excess androgen production is encouraged by hyperinsulinemia which causes obesity irregular menstruation and infertility. These anomalies may eventually lead to endometrial cancer diabetes mellitus cardiovascular disease and atherosclerosis (12). Therefore lowering long-term complications requires early detection of metabolic abnormalities. An elevated risk of diabetes is indicated by an HbA1c value of 5. 7 percent or higher. HbA1c may also be an indicator of risk in cardio-vascular diseases in female with PCOS according to earlier research that showed strong

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correlations between HbA1c levels body mass index and lipid abnormalities (13). HbA1c is still a useful and accessible screening tool in standard clinical settings despite some studies casting doubt on its ability to diagnose impaired glucose tolerance. In comparison to healthy the current study showed that ladies with PCOS had considerably higher BMI HbA1c percentage and insulin resistance. Significant insulin resistance was confirmed in PCOS patients by elevated HOMA-IR values. Serum levels of AMH and testosterone were also markedly elevated indicating the hormonal abnormalities frequently linked to the syndrome. Although variations in LH TSH and prolactin levels were noted there was no discernible difference in these parameters between the groups. There is mounting evidence that (IR) insulin resistance is closely combined with metabolic syndrome and exists across various PCOS phenotypes. As a result long-term metabolic problems are a significant health concern and PCOSs reproductive symptoms may only account for a small percentage of the diseases burden (14). Our studys results reinforce the significance of evaluating metabolic risk factors in PCOS-affected women especially those with high HbA1c levels. HbA1c testing is advised by the American Diabetes Association as a standard technique for assessing glucose regulation and identifying people at risk for diabetes. Elevated HbA1c levels have been linked to metabolic abnormalities in PCOS in a number of studies indicating its potential utility in risk assessment and clinical evaluation (15). Our results support these findings and indicate that HbA1c may be a useful marker for identifying PCOS-affected women who are more likely to develop insulin resistance and cardiometabolic disease in the future. The mainstay of PCOS treatment is still lifestyle modification. Reducing weight improving diet and engaging in regular exercise can increase insulin sensitivity lessen excess androgen and improve reproductive outcomes. The long-term burden of diabetes and cardiovascular disease may also be lessened by early detection and suitable intervention. The current study has some restrictions. The study was carried out over a two-year period at a single center which might restrict how broadly the results can be applied. To better understand the connection between HbA1c metabolic risk and insulin

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resistance in women with PCOS larger multicenter studies with a variety of populations are required.

Conclusion:

Study concluded that when compared to healthy controls women with PCOS had much higher rates of obesity irregular menstruation hyperandrogenic features elevated HbA1c levels and insulin resistance. The results show that HbA1c is a straightforward affordable and clinically useful marker for detecting metabolic dysfunction and possible cardiovascular risk in PCOS-affected women. Early identification of people with elevated cardiometabolic risk may be aided by an HbA1c value of roughly 5. 3%. Therefore to improve long-term health outcomes for women with PCOS regular metabolic screening prompt intervention and a multidisciplinary management approach are crucial.

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