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Predictable Clinical Indicators for Endometrial Illness and Endometrial Histology in Patients with Polycystic Ovarian Syndrome

Dr Shagufta Naz[1*], Dr Anila Shah Bukhari[2], Dr Abdul Hafeez Khan[3], Dr Bushra Nabi[4], Dr Shahid Fareed[5], Dr Samina Amin[6]

[1*]Ex TMO, Department of Obstetrics and Gynaecology, Hayatabad Medical Complex, Peshawar, Pakistan
[2]Assistant Professor, Department of Anatomy, Rehman Medical College, Peshawar, Pakistan
[3]Assistant Professor, Department of Anatomy, Khyber Medical College, Peshawar, Pakistan
[4]Assistant Professor, Department of Obstetrics and Gynaecology, Bannu Medical College, Bannu, Pakistan
[5]Assistant Professor, Department of Anatomy, Rehman Medical College, Peshawar, Pakistan
[6]Registrar, Department of Obstetrics & Gynaecology, Northwest General Hospital, Peshawar, Pakistan

***Corresponding author's email address:** sk6005047@gmail.com

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ABSTRACT

Background: 'Polycystic ovarian syndrome (PCOS) is a prevalent endocrine disorder among women of reproductive age'. 'It is characterized by hyperandrogenism, menstrual irregularities, and metabolic dysfunction, which predispose patients to endometrial abnormalities'. Despite extensive research on its metabolic and reproductive effects, the relationship between PCOS and endometrial pathology requires further exploration. The objective was to evaluate the clinical, hormonal, metabolic, and histological indicators of endometrial abnormalities in women with PCOS and compare them to healthy controls.

Methodology: A cross-sectional study was conducted at Hayatabad Medical Complex, including 120 participants divided into two groups: 60 'women with PCOS diagnosed based on Rotterdam criteria and 60 healthy controls'. Data collection involved clinical evaluation, hormonal and metabolic profiling, ultrasound assessment, and histological examination of endometrial biopsies. 'Statistical analysis was performed using SPSS version 25, with significance set at $p < 0.05$'.

Results: 'Women with PCOS had significantly higher BMI (30.2 ± 5.8 vs. 24.7 ± 4.6; '$p < 0.001$)' and menstrual irregularities (83% vs. 12%; $p < 0.001$). Hormonal and metabolic markers, including LH/FSH ratio (2.9 ± 1.2 vs. 1.3 ± 0.4; $p < 0.001$), estradiol (63.2 ± 14.5 vs. 49.5 ± 11.8 pg/mL; $p < 0.001$), and HOMA-IR (4.3 ± 1.6 vs. 2.2 ± 0.8; $p < 0.001$), were significantly elevated in the PCOS group. Endometrial thickness was greater in women with PCOS (12.5 ± 3.3 mm vs. 8.9 ± 2.6 mm; $p < 0.001$). Histological abnormalities, including hyperplasia with atypia (15% vs. 2%; $p < 0.001$) and endometrial carcinoma '(5% vs. 0%; $p = 0.014$), were more prevalent in the PCOS group'.

Conclusion: Women with PCOS are at a higher risk of endometrial abnormalities due to hormonal and metabolic disturbances. Early screening and intervention targeting these risk factors can mitigate the potential for severe endometrial pathologies, including malignancies. Further research should explore the progression of endometrial changes in PCOS and the efficacy of targeted therapeutic approaches.

Keywords: Polycystic ovarian syndrome (PCOS), Endometrial abnormalities, Hyperplasia, Hormonal imbalance, Insulin resistance, Endometrial carcinoma, Menstrual irregularities, Metabolic dysfunction, Rotterdam criteria, Endometrial thickness.

Introduction

Polycystic ovarian ‘syndrome (PCOS) is a common endocrine disorder that affects women of reproductive age, with its prevalence varying from 6% to 20% globally, depending on the criteria used for diagnosis’ (1, 2). The condition is defined by a combination of clinical features, including hyperandrogenism, menstrual irregularities, and the presence ‘of polycystic ovaries on ultrasound’. PCOS is not only a leading cause of infertility but is also associated with significant metabolic disturbances and long-term health risks, including abnormalities in endometrial function(3).

A key concern in women with PCOS is chronic anovulation, which results in prolonged exposure to unopposed estrogen (4). This hormonal imbalance disrupts the normal cyclical development of the endometrium, increasing the risk of pathological changes such as endometrial hyperplasia and, in severe cases, endometrial carcinoma. Additional factors, such as obesity, insulin resistance, and hyperinsulinemia, further amplify these risks, highlighting the complex interaction between metabolic and reproductive health in PCOS (5).

Despite extensive research into the metabolic and reproductive aspects of PCOS, its effects on endometrial health remain underexplored. Identifying clinical, hormonal, and metabolic predictors of endometrial abnormalities in women with PCOS can aid in early detection and risk assessment. ‘This study aims to evaluate the relationship between clinical features, metabolic markers, and histological changes in the endometrium of women with PCOS compared to healthy controls’. By enhancing our understanding of these associations, the study seeks ‘to improve the management of endometrial risks in women with PCOS and guide preventive strategies’.

Methodology:

‘This cross-sectional study was conducted at the Hayatabad Medical Complex’, a tertiary care hospital, from January 2023 to January 2024 to evaluate the clinical, hormonal, metabolic, and histological indicators of endometrial abnormalities ‘in women with polycystic ovarian syndrome (PCOS) compared to’ normal individuals. ‘A total of 120 participants were included, divided into two equal groups: 60 women diagnosed with PCOS based on the Rotterdam criteria and 60 healthy women with no clinical or biochemical evidence of PCOS, who served as controls’. The study was conducted for one year, with participants recruited from the gynaecology outpatient clinic.

Women aged 18 to 40 years were eligible to participate. The PCOS group included women who met at least two of the following Rotterdam criteria: oligo- or anovulation, clinical or biochemical hyperandrogenism, or polycystic ovaries detected on ultrasound. The control group included women with regular menstrual cycles and no clinical or hormonal abnormalities. Exclusion criteria for both groups included hormonal treatment, a history of endometrial carcinoma, pregnancy, or chronic illnesses such as diabetes, thyroid disorders, or hypertension.

Data collection involved clinical evaluation, hormonal and metabolic profiling, ultrasound examination, and histological assessment of endometrial samples. Clinical data included menstrual history, parity, and age at menarche. Physical examination focused on body mass index (BMI) and signs of hyperandrogenism, such as hirsutism and acne. The hormonal analysis included measurements of luteinizing hormone (LH), follicle-stimulating hormone

(FSH), estradiol, and anti-Müllerian hormone (AMH). Metabolic parameters assessed were 'fasting blood glucose, fasting insulin, triglycerides, and HOMA-IR (Homeostasis Model Assessment of Insulin Resistance)'.

Transvaginal ultrasounds were performed to measure endometrial thickness and identify polycystic ovarian morphology. Endometrial biopsies were collected during the proliferative phase of the menstrual cycle or its equivalent in cases of irregular cycles. Histological findings were categorized as normal proliferative or secretory phase, simple or complex hyperplasia (with or without atypia), or endometrial carcinoma.

The data were analyzed using SPSS version 25. Continuous variables were presented as means with standard deviations and compared between groups using the Student's t-test. Categorical variables were expressed as percentages and analyzed with the chi-square test. 'A p-value of less than 0.05 was considered statistically significant'. Multivariate logistic regression was performed to identify independent predictors of abnormal histology, adjusting for confounding factors such as BMI and insulin resistance. Results were expressed as odds ratios with 95% confidence intervals.

Result:

The analysis of demographic and clinical characteristics revealed significant differences between the PCOS and normal groups. While the average age of participants in both groups was similar (**p = 0.410**), BMI was significantly higher in the PCOS group compared to the normal group (**p < 0.001**). This aligns with the established association between obesity and PCOS. Additionally, menstrual irregularity was significantly more prevalent among women with PCOS (**p < 0.001**), highlighting its diagnostic importance and its potential role in endometrial abnormalities. Parity was slightly lower in the PCOS group, reflecting potential fertility issues commonly associated with the condition (**p = 0.018**). However, the age at menarche 'did not differ significantly between the groups (**p = 0.102**)', suggesting that puberty onset timing may not influence the development of PCOS-related endometrial changes.

Table 1: Demographic and Clinical Characteristics of the Study Groups

Variable	PCOS Group (n=60)	Normal Group (n=60)	p-value
Age (years)	27.6 ± 5.1	28.3 ± 4.8	0.410 (NS)
BMI (kg/m²)	30.2 ± 5.8	24.7 ± 4.6	<0.001 (S)
Menstrual Irregularity (%)	83%	12%	<0.001 (S)
Parity (number)	0.8 ± 0.5	1.1 ± 0.6	0.018 (S)
Menarche Age (years)	12.8 ± 1.4	13.2 ± 1.2	0.102 (NS)

Hormonal and metabolic profiles differed significantly between the PCOS and normal groups. 'The LH/FSH ratio was markedly higher in the PCOS group' (**p < 0.001**), reflecting the hormonal imbalance characteristic of PCOS. Estradiol 'levels were also significantly elevated in the PCOS group (**p < 0.001**)', likely due to unopposed estrogen exposure. Anti-Müllerian hormone (AMH), a marker of ovarian reserve, was significantly higher in women with PCOS (**p < 0.001**), consistent with increased follicular activity. Metabolic parameters also showed significant differences; fasting insulin levels and HOMA-IR scores were elevated in the PCOS group (**p < 0.001**), indicating higher insulin resistance. Triglyceride levels were also

significantly higher in PCOS patients (**p < 0.001**), reinforcing the link between PCOS and metabolic syndrome.

Table 2: Hormonal and Metabolic Profiles

Parameter	PCOS Group (n=60)	Normal Group (n=60)	p-value
LH/FSH Ratio	2.9 ± 1.2	1.3 ± 0.4	<0.001 (S)
Estradiol (pg/mL)	63.2 ± 14.5	49.5 ± 11.8	<0.001 (S)
AMH (ng/mL)	8.5 ± 3.0	3.4 ± 1.2	<0.001 (S)
Fasting Insulin (µIU/mL)	18.7 ± 5.2	10.2 ± 3.4	<0.001 (S)
HOMA-IR	4.3 ± 1.6	2.2 ± 0.8	<0.001 (S)
Triglycerides (mg/dL)	170.4 ± 35.6	130.5 ± 25.8	<0.001 (S)

Endometrial thickness was significantly greater in women with PCOS compared to the normal group (**p < 0.001**), which may indicate a higher risk for endometrial hyperplasia and other abnormalities. Histological analysis showed stark differences between the two groups. Women with PCOS had lower rates of normal proliferative and secretory phase endometrium (**p < 0.001** for both), while simple and complex hyperplasia were more common in this group (**p < 0.001** and **p = 0.005**, respectively). Notably, hyperplasia with atypia and endometrial carcinoma were significantly more prevalent in the PCOS group (**p < 0.001** and **p = 0.014**, respectively), underlining the increased risk of endometrial pathology in these patients.

Table 3: Endometrial Thickness and Histological Abnormalities

Variable	PCOS Group (n=60)	Normal Group (n=60)	p-value
Endometrial Thickness (mm)	12.5 ± 3.3	8.9 ± 2.6	<0.001 (S)
Normal Proliferative Phase	38%	80%	<0.001 (S)
Normal Secretory Phase	22%	75%	<0.001 (S)
Simple Hyperplasia	23%	7%	<0.001 (S)
Complex Hyperplasia	12%	3%	0.005 (S)
Hyperplasia with Atypia	15%	2%	<0.001 (S)
Endometrial Carcinoma	5%	0%	0.014 (S)

When comparing normal and abnormal histology, several factors showed significant correlations. Women with abnormal histology had a higher BMI (**p < 0.001**) and greater endometrial thickness (**p < 0.001**) compared to those with normal histology, emphasizing their role as predictive indicators. Hormonal imbalances, including a higher LH/FSH ratio (**p < 0.001**) and elevated HOMA-IR scores (**p < 0.001**), were more pronounced in the abnormal histology group. Notably, hyperplasia with atypia was exclusively observed in 35% of the abnormal histology group (**p < 0.001**), indicating its importance as a risk factor for malignancy.

Table 4: Correlation of Clinical and Hormonal Factors with Histopathology

Factor	Normal Histology (n=80)	Abnormal Histology (n=40)	p-value
BMI (kg/m²)	26.5 ± 4.3	32.1 ± 6.0	<0.001 (S)
Endometrial Thickness (mm)	9.3 ± 2.5	13.6 ± 3.1	<0.001 (S)
LH/FSH Ratio	1.8 ± 0.6	2.7 ± 1.1	<0.001 (S)
HOMA-IR	2.4 ± 1.0	4.5 ± 1.3	<0.001 (S)
Hyperplasia with Atypia (%)	0%	35%	<0.001 (S)

S: Statistically Significant and **NS**: Not Significant

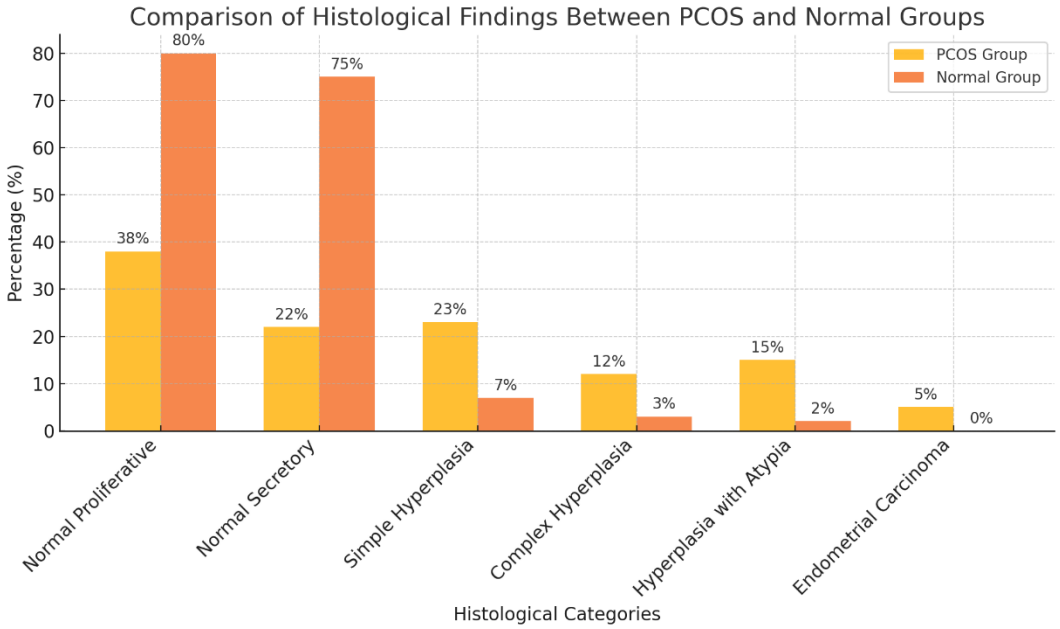

Figure 1: The bar chart shows significantly lower rates of normal proliferative (38%) and secretory phase (22%) endometrium in the PCOS group compared to the normal group (80% and 75%, respectively). Simple and complex hyperplasia were more frequent in PCOS (23% and 12%) than in the normal group (7% and 3%). Notably, hyperplasia with atypia (15%) and endometrial carcinoma (5%) were observed only in the PCOS group, highlighting their increased risk for endometrial abnormalities and malignancy.

Discussion

This study provides valuable insights into the clinical, hormonal, metabolic, and histological characteristics of women with PCOS compared to healthy controls. The findings highlight the significant impact of PCOS on endometrial health and the associated risk factors for

endometrial abnormalities. These results align with and expand upon existing literature, reinforcing the need for vigilant monitoring and management of endometrial risks in women with PCOS.

The higher BMI observed in the PCOS group compared to the controls aligns with studies that consistently link obesity to PCOS (6, 7). Obesity exacerbates insulin resistance, a hallmark of PCOS, and contributes to hyperinsulinemia, which promotes androgen excess and disrupts normal endometrial function. Similar to previous studies, found significantly elevated fasting insulin and HOMA-IR levels in women with PCOS (8, 9). These findings underline the intertwined relationship between metabolic dysfunction and reproductive health in PCOS.

Menstrual irregularities, observed in 83% of women with PCOS, were consistent with the chronic anovulation characteristic of the syndrome. Studies have also reported a high prevalence of oligomenorrhea or amenorrhea in PCOS, emphasizing its role in prolonged estrogen exposure and subsequent endometrial abnormalities (10-12).

The elevated LH/FSH ratio and higher levels of estradiol in women with PCOS 'observed in this study are consistent with findings from previous research'. Studies reported that women with PCOS often exhibit hormonal imbalances, including elevated LH/FSH ratios and persistent estradiol levels, which disrupt normal endometrial development (13, 14). Elevated anti-Müllerian hormone (AMH) levels observed in the PCOS group further corroborate earlier studies suggesting increased follicular activity in these patients.

The significantly greater endometrial thickness in the PCOS group compared to the control group highlights the risk of hyperplasia and other endometrial abnormalities in these women. Similar studies found that prolonged unopposed estrogen exposure in PCOS leads to increased endometrial thickness and higher rates of endometrial hyperplasia (15, 16).

The histological analysis in the present study 'showed a higher prevalence of hyperplasia' (both simple and complex) and hyperplasia with atypia in the PCOS group, consistent with earlier studies (16, 17). Notably, the presence of endometrial carcinoma in 5% of women with PCOS in this study underscores the increased malignancy risk in this population, as highlighted in studies (18).

The stark differences in normal endometrial phases (proliferative and secretory) between the PCOS and control groups highlight the significant disruption of endometrial homeostasis in PCOS. While 80% of the control group exhibited normal proliferative endometrium, only 38% of the PCOS group did. Similarly, the secretory phase was present in 75% of controls but only 22% of the PCOS group. These differences align with studies that reported that chronic anovulation in PCOS impairs the transition to the secretory phase, leading to abnormal endometrial proliferation (19, 20).

The findings of this study emphasize the importance of early identification and management of risk factors for endometrial abnormalities in women with PCOS. Routine assessment of endometrial thickness, combined with hormonal and metabolic evaluation, should be integrated into the clinical care of these patients. Additionally, addressing modifiable risk factors, 'obesity and insulin resistance, could reduce the risk of endometrial pathology'.

'Future research should focus on longitudinal studies to' better understand the progression of endometrial abnormalities in PCOS and the role of targeted interventions in reducing these

risks. Exploring the molecular pathways involved in endometrial changes in PCOS could also provide insights into novel therapeutic strategies.

Conclusion

This study reinforces the significant association between PCOS and endometrial abnormalities, highlighting the critical role of hormonal and metabolic factors in driving these changes. The findings underscore 'the need for a comprehensive approach to the management' of endometrial risks in women with PCOS, including regular monitoring, lifestyle modifications, and early interventions. These measures 'are essential to improving reproductive health outcomes and reducing the risk of endometrial malignancies in this high-risk population'.

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