International Journal of Reproduction, Contraception, Obstetrics and Gynecology
*Thyagaraju C et al. Int J Reprod Contracept Obstet Gynecol. 2026 Feb;15(2):642-650*
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20260186

**Original Research Article**

# Endometrial hysteroscopic and histopathological characteristics in infertile women with polycystic ovary syndrome versus unexplained infertility: a comparative cross-sectional study

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**Received:** 02 January 2026
**Revised:** 14 January 2026
**Accepted:** 16 January 2026

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## ABSTRACT

**Background:** Polycystic ovary syndrome (PCOS) affects 5-15% of reproductive-aged women and accounts for nearly 90–95% of anovulatory infertility. Beyond ovulatory dysfunction, PCOS is associated with insulin resistance, obesity, chronic inflammation, and increased metabolic and atherogenic risk. These factors predispose to endometrial dysfunction, hyperplasia, and carcinoma, contributing to implantation failure and miscarriage. Hence, evaluation of endometrial abnormalities in PCOS is essential for comprehensive infertility management. Aim of the study was to compare hysteroscopy and histopathological endometrial findings in infertile women with PCOS and unexplained infertility (UI), and to correlate clinical and hormonal profiles between the groups.
**Methods:** A cross-sectional analytical study conducted over two years in a tertiary care obstetrics and gynecology center. A total of 165 infertile women were included (85 with PCOS, 80 with UI). After informed consent, detailed clinical evaluation was performed. Hormonal profile and pelvic ultrasound were done on day 2 of menstruation. Diagnostic laparoscopy, hysteroscopy, laparoscopic ovarian cautery (where indicated), and endometrial biopsy were performed. Clinical, hormonal, hysteroscopic, and histopathological findings were compared between both the groups. Statistical analysis was done using statistical package for the social sciences (SPSS) v26; $p<0.05$ was considered significant.
**Results:** Women with PCOS were younger and had significantly higher BMI and longer duration of infertility than UI ($p<0.05$). Day-2 endometrial thickness was significantly higher in PCOS (7.5±1.8 mm versus 5.6±1.7 mm). Hysteroscopy was normal in 82% of PCOS and 70% of UI women. Micropolyps and hyperemic endometrium were more frequent in PCOS, while polyps, adhesions, and uterine anomalies predominated in UI. Histologically, PCOS showed higher rates of proliferative and disordered proliferative endometrium, with endometrial hyperplasia detected in 8.4%, compared to none in UI.
**Conclusions:** Normal hysteroscopic findings do not reliably indicate a normal endometrial milieu in PCOS. Routine endometrial biopsy alongside hysteroscopy may uncover subclinical pathology and improve infertility management in this population.

**Keywords:** PCOS, Unexplained Infertility, Hysteroscopy, Histopathology, Endometrium, Comparative study

## INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrine disorder involving multiple systems affecting around 5 to 15 % of females in reproductive age group and it contributes to 90-95 % of anovulatory infertility Different groups classify PCOS differently because of the heterogenous nature of the disease.[1] The exact aetiology and pathogenesis of PCOS is still an area of active research and multiple hypotheses have been postulated, ranging from genetic susceptibility to environmental exposure in utero and also in the postnatal life.

In a recent study done in our institution in 2018, the prevalence of metabolic syndrome (MeS) which includes central obesity, hypertension, insulin resistance and atherogenic dyslipidaemia in women with PCOS was 42% compared to 19% in women without PCOS features.[2] Chronic inflammation in these women accelerates atherogenesis and hypertension due to increased levels of insulin and free fatty acids. Prolonged unopposed estrogen, hyperinsulinemia, and elevated levels of free insulin, growth factor-1, and androgens increase the proliferative activity of the endometrium, resulting in hyperplasia and carcinoma acceleration.[3] But this risk is still frequently overlooked by the doctors giving treatment for these women.[4] The management of women with PCOS should include not only the reproductive function of the female, but also early diagnosis of metabolic syndrome which are contributing to development of endometrial hyperplasia and endometrial cancer.

In patients with PCOS there is higher rate of implantation failure after induction of ovulation or spontaneous miscarriage after pregnancy which is not only due to anovulation but also due to endometrial dysfunction. Several studies have assessed the etiology of anovulation resulting in infertility in these women; however, studies on the endometrium of women with PCOS are limited. Therefore, the features of the endometrial abnormalities in women with PCOS has to be reviewed in order to increase the reproductive outcome in these women.[5]

Several studies have been done on prevalence of endometrial hyperplasia and endometrial cancer in women with PCOS in comparison to general population varies from 0 to 20%.[6-8] The exact risk in these women is contradictory in various studies.[9] There is still no clear evidence that PCOS is an independent risk factor for endometrial hyperplasia or pathology.

This study is aimed to evaluate the endometrium of the infertile women with PCOS and compare it with women with unexplained infertility and assess its relationship with clinical and hormonal patterns between both the groups.

## METHODS

This study was an analytical cross-sectional study conducted at our tertiary care hospital JIPMER, Pondicherry for period of 3 years from January 2019 to January 2022. Due to COVID, the study was extended by one year up to Jan 2023. The study was approved from the institute ethics committee (JIP/IEC/2019/184) and funded by institute intramural grant for research.

Research was performed according to the 'World Medical Association Declaration of Helsinki ethical principles for medical research involving human subjects. Written informed consent was obtained from all participants during the enrolment into the study.

### *Inclusion criteria*

Infertile PCOS women according to Rotterdam 2003 criteria and infertile women with unexplained infertility (regular cycles, patent fallopian tubes, normal semen analysis) diagnosis attending infertility clinic in our institute were recruited.

### *Exclusion criteria*

Infertile women with hypo/hyperthyroidism (deranged TSH and FT4 levels) or other endocrine abnormalities such as congenital adrenal hyperplasia, adrenal tumours, Cushing syndrome, women on oral contraceptive pills and corticosteroids were excluded.

Sample size was calculated using n Master (Version 2.0) at 95% confidence interval, 80% power, and assuming the risk difference of 13.5% (proportion of endometrial hyperplasia among PCOD and non PCOD women is 18.5% and 5% respectively, the required sample size per group was 85. 85 women in each group were enrolled.

### *Study procedure*

Patients fulfilling the inclusion criteria and willing to participate in our study were recruited from the Infertility clinic of OBG department JIPMER after obtaining informed consent. After the initial workup of the patient, the patient was counselled about the procedure to be done, consent was taken. She was advised to come on day 2 of menses for baseline transvaginal ultrasonography. A comprehensive infertility workup of the patients including a detailed history, clinical examination of both the partners and investigations were done. Detailed history of patients was taken including age of the patient, duration of Infertility, knowledge of fertile period, duration of married life, history of galactorrhoea, dysmenorrhea, dyspareunia, whether cycles are regular or irregular, history of thyroid disorder, diabetes mellitus or any other medical disorders were taken. Previous treatment history- usage of ovulation induction drugs, duration of ovulation drugs intake, any history of previous pelvic surgeries or any fertility enhancing surgeries were noted. In case of secondary infertility, detailed history of previous pregnancies and details of any post-abortal or puerperal sepsis was noted specifically. Male partner history includes age, occupation, any medical disorder, history of smoking and

alcoholism. Any history suggestive of mumps in childhood, testicular trauma, pelvic surgery and occupational exposure to hazardous substances were noted.

Clinical examination includes general physical examination measuring height, weight, BMI, blood pressure, breast examination, look for presence of hirsutism, galactorrhoea and thyroid enlargement. Abdominal examination was done to rule out the presence of any abdominal or pelvic mass. Speculum examination was done to look for cervical or vaginal discharge and any cervical lesions.

Vaginal examination was done to look for uterine size, mobility, tenderness, presence of any adnexal mass and nodularity in the posterior fornix. Husband was examined to look for local lesions like hydrocoele, varicocele, previous surgical scars particularly pelvic surgeries.

Following investigations were done- complete blood count on day 2 of menstrual cycle (processed in Sysmex analyser), serum T3, T4, TSH levels on day 2 of menstrual cycle (Unicel Dxl immunoassay system), serum FSH, serum LH, serum prolactin, serum testosterone levels on day 2 of menses was done by immunoassay (Unicel Dxl immunoassay system), baseline transvaginal ultrasonography using mindray machine on day 2 of menses was done to look for PCOS morphology, endometrial thickness, antral follicular count, ovarian volume and to detect any uterine abnormalities, tubal patency either by hysterosalpingogram or HyCosy or Chromotubation in hystero-laparoscopy and husband semen analysis (using 2022 WHO semen analysis criteria).

***Diagnostic hysterolaparoscopy***

For indicated hysterolaparoscopy, the patients were admitted the previous day and it was performed in the proliferative phase of the cycle (day 6 to day 10) and for OPD diagnostic hysteroscopy, patient was called on the day of the surgery and in was done under mild sedation and paracervical block.

***Diagnostic hysteroscopy procedure***

Hysteroscope was introduced intracervically, with distension media as normal saline and panaromic view of the uterine cavity and bilateral ostia visualised. Any endometrial pathology present was noted and endometrial biopsy was taken for all patients. Hysteroscopy findings and endometrial biopsy report was collected for patients.

***Statistical analysis***

Data was entered into Microsoft excel data sheet and was analyzed using statistical package for the social sciences (SPSS) 20 version software. Categorical data was represented in the form of Frequencies and proportions. Chi- square was used as test of significance. Continuous data was represented as mean and standard deviation. The normality of data was analyzed using the Kruskal-Walli's test, and because the clinical parameters did not show a normal distribution, the Mann-Whitney U test/ Independent t test was used to compare the quantitative data between the two groups. $p<0.05$ was considered as statistically significant.

## RESULTS

Table 1 shows the demography characteristics of all participants. The Mean age was significantly lower and BMI was significantly higher in the PCOS group than in the UI group (both $p<0.001$). The prevalence of obesity and overweight was 20.8% and 52.2% in the PCOS group and 1.7% and 15% in the UI group, respectively. PCOS patients had longer duration of infertility compared to Unexplained infertility patients and it was statistically significant($p<0.021$). Irregular menstruation and hyperandrogenic clinical symptoms were more in PCOS women compared to UI group and it was significant($p<0.034$). The median endometrial thickness on day 2 of menstrual cycle was higher in women with PCOS compared to UI (7.5±1.8 versus 5.6±1.7) respectively and was statistically significant.

Patients in the UI group patients had normal TSH, LH, FSH, and testosterone levels, whereas those in the PCOS group had different levels of these hormones, and there were significant differences in LH and testosterone levels between the groups ($p<0.001$) (Table 2). The results of the Mann-Whitney test showed the LH/FSH ratio was higher in the PCOS group than in the UI group (2.2±1.6 versus 1.1±0.6, respectively, $p<0.001$). Impaired glucose test was seen in 46.2% patients in PCOS group compared to 23% in Unexplained infertility group and it was statistically significant ($p<0.002$).

Hysteroscopic findings revealed normal findings in 70 patients (82%) in the PCOS group, hyperplastic endometrium in 3 patients, hyperemic in 7 patients and micropolyps in 5 patients (5.8%). In unexplained infertility group, 70% of women had normal hysterscopic findings, The most common abnormality detected in hysteroscopy was uterine polyp (8.1%), intrauterine adhesions (9.9%) and sub-septate uterus (9.3%) (Table 3).

**Table 1: The demographic characteristics of patients in the PCO and UI groups.**

| Characteristics | Group A (PCOS) n=85 | Group B (unexplained) n=85 | P value |
|---|---|---|---|
| **Age (years)** | 26.50±3.50 | 30.00±3.10 | <0.001 |
| **Body mass index (kg/m$^2$)*** | 26.70±3.40 | 22.10±3.00 | <0.001 |

Continued.

| Characteristics | Group A (PCOS) n=85 | Group B (unexplained) n=85 | P value |
|---|---|---|---|
| **Primary infertility (%)** | 53.5 | 45.5 | 0.305 |
| **Duration of infertility (years)*** | 5.5±3.10 | 4.0±1.90 | 0.021 |
| **Metformin consumption (%)** | 51.5 | 15.7 | <0.001 |
| **OCPs (%)** | 74.6 | 16 | <0.001 |
| **Oligomenorrhea* (%)** | 75.5 | 16.6 | 0.034 |
| **Hirsutism (%)** | 34.3 | 10.3 | <0.001 |
| **Acne (%)** | 38.8 | 13 | <0.001 |
| **Endometrial thickness (mm)/D$^2$** | 7.5±1.8 | 5.6±1.7 | <0.001 |
| **Ovarian volume (>10 ml) (%)** | 49.1 | 0 | <0.001 |

*Data presented as mean ± SD, data presented as percentage, p value is calculated by Chi-square test.

**Table 2: Comparison of hormonal profile between the two groups.**

| Variables | Categories | Group A, n=85 (%) | Group B, n=85 (%) | P value |
|---|---|---|---|---|
| | | PCOS | UI | |
| **FSH (IU/l)** | Normal | 76 (89.7) | 52 (94.5) | 0.491 |
| | Elevated | 9 (10.3) | 3 (5.5) | |
| **LH (IU/l)** | Normal | 61(71.2) | 49 (89.1) | 0.017* |
| | Elevated | 24 (28.8) | 6 (10.9) | |
| **TSH (mIU/l)** | Normal | 71(83.1) | 48 (85.7) | 0.694 |
| | Elevated | 14(16.9) | 8 (14.3) | |
| **Prolactin (mIU/l)** | Normal | 85(100) | 85 (100) | |
| | Elevated | 0 | 0 | |
| **Testosterone (ng/dl)** | Normal | 63 (74.6) | 55 (91.66) | <0.001* |
| | Elevated | 22 (25.4) | 0 (0) | |

*p value is calculated by Mann-Whitney test.

**Table 3: Hysteroscopy findings between both the groups.**

| Characteristics | Group A (PCOS), n=85 (%) | Group B (unexplained), n=85 (%) |
|---|---|---|
| **Normal** | 70 (82) | 65 (76) |
| **Hyperplasia endometrium** | 3 (3.5) | 0 |
| **Hyperemeic endometrium** | 6 (8.2) | 0 |
| **Endometrial polyps** | 1 (1.2) | 7 (8.2) |
| **Intrauterine adhesions** | 0 | 9 (10.5) |
| **Micropolyps** | 5 (5.9) | 1 (1.2) |
| **Subseptate uterus** | 0 | 8 (9.3) |

**Table 4: Comparison of histopathology findings in between both the groups.**

| Endometrial pattern | Total, n=170 (%) | Group A PCOS (n=85) (%) | Group B UI (n=85) (%) | P value |
|---|---|---|---|---|
| **Proliferative** | 64 (37.3) | 41 (48.2) | 23 (27) | <0.001* |
| **Disordered proliferative** | 15(8.8) | 15(17.6) | 0 | <0.001* |
| **Secretory** | 62 (36.5) | 14 (16.5) | 48 (56.5) | <0.001* |
| **Endometrial polyp** | 11(6.5) | 4(4.7) | 7(8.2) | 0.835 |
| **Chronic endometritis** | 3(1.57) | 2 (2.3) | 1 (1.16) | 0.968 |
| **Endometrial hyperplasia** | 7 (5.55) | 7 (8.2) | 0 | <0.001* |
| **Endometrial tuberculosis** | 1 (0.78) | 0 | 1 (1.16) | 0.543 |
| **Insufficient sample** | 7(4.72) | 2 (2.3) | 5 (5.8) | 0.943 |

Data presented as percentage, Chi-square test; *p value is calculated by Chi-square test.

There was a significant difference in histological findings between the PCOS and UI groups (p<0.001) (Table 4). On histopathology, proliferative endometrium (Figure 1) was found more in women with PCOS (48.7%) compared to unexplained group (27%). Disordered proliferative endometrium was found in 17.6% of women in PCOS

group compared to none in unexplained infertility group. Secretory endometrium was found more in women with unexplained infertility (56%) compared to women with PCOS (16.8%). Endometrial hyperplasia (Figure 2) was detected in 7 patients (5.5%) in with PCOS compared to none in UI group. Endometrial polyps (Figure 3) and Chronic endometritis (Figure 4) was seen in 6.5% and 1.5% respectively.

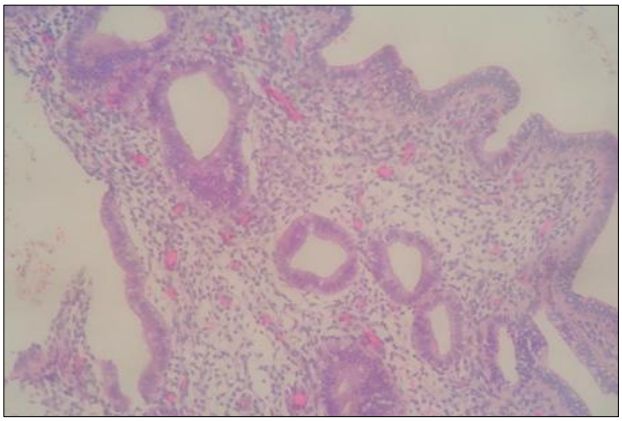

**Figure 1: Proliferative endometrium on HPE.**

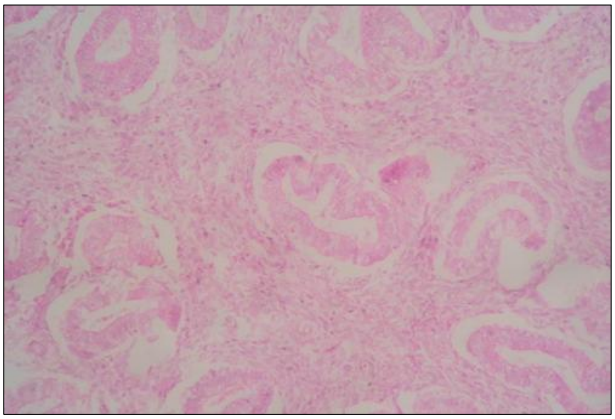

**Figure 2: Endometrial hyperplasia on HPE.**

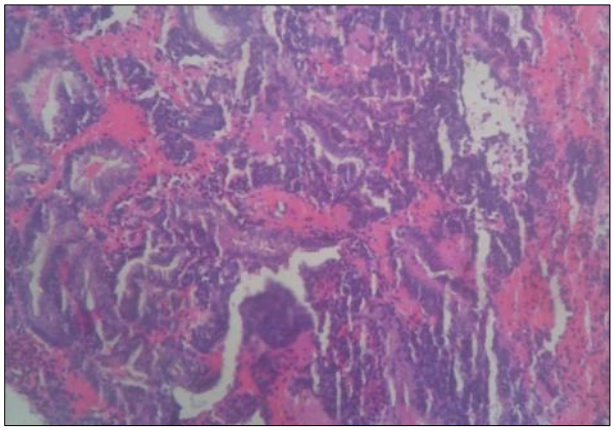

**Figure 3: Endometrial leimyomatous polyp on HPE.**

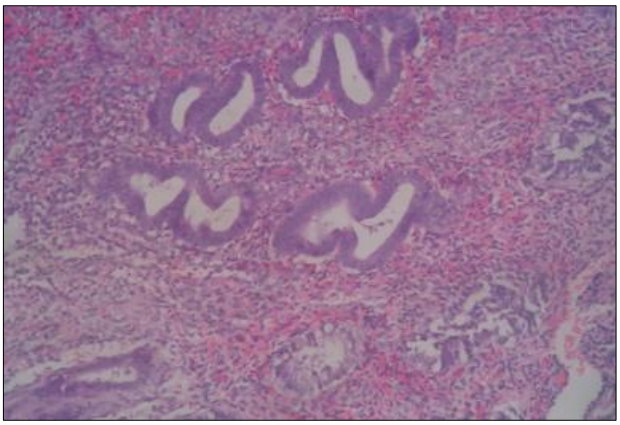

**Figure 4: Chronic endometritis features on HPE.**

## DISCUSSION

In women with PCOS, there is prolonged anovulation causing consequent continued secretion of estrogen unopposed by progesterone which increases risk of endometrial abnormalities like endometrial hyperplasia, and endometrial cancer particularly in young women. RCOG guidelines recommends to induce withdrawal bleed in PCOS patients every 3 to 4 months with gestogens because these women due to this increased risk and recommends hysteroscopy and/or endometrial biopsy if thickened endometrium or an endometrial polyp.[10]

The mean age of women with PCOS was lower than women with unexplained infertility (p=0.007) in our study which was similar to studies done by Amooee et al Indhavivadhana et al and Ramezanali et al.[9,11,12] Alterations in ovarian morphology, elevated androgen levels, ovulatory dysfunction, and obesity can contribute to delayed conception and prompt earlier clinical consultation among women with PCOS. The mean Body mass index of the PCOS group observed in our study was 26.70±3.40 compared to 22.10±3.00 in unexplained infertility group, which was similar to the studies by Al-Jefout et al, Amooee et al, Indhavivadhana et al and Ramezanali et al.[6,9,11,12] In women with PCOS, obesity and elevated BMI are driven by androgen-mediated alterations in lipolysis, insulin resistance with compensatory hyperinsulinemia, and increased steroidogenesis. Obesity is additionally associated with heightened LH secretion, which further contributes to anovulatory cycles in PCOS.[13] Hyperandrogenism is also known to increase visceral obesity due to its peripheral action on adipose tissue in women with PCOS.[14] The mean duration of infertility in our group was more in PCOS group which was consistent with study by Amooee et al.[9] The reason might be primarily because of anovulation, LH dysfunction, arrest of follicular maturation and associated increased risk of metabolic syndrome leading to decreased response to infertility treatment compared to women without PCOS.

Menstrual disturbances, particularly oligomenorrhoea, were observed to be significantly more prevalent among

women with polycystic ovary syndrome (PCOS) compared to their Unexplained counterparts (p=0.034). This observation aligns with the findings of Ramezanali et al and Al-Jefout et al.[6,12] who similarly reported a higher frequency of menstrual irregularities in women diagnosed with PCOS. The pathophysiological basis for this association lies in the chronic anovulation, insulin resistance, and hypoestrogenism characteristic of PCOS, which, when unopposed by progesterone, predispose the endometrium to proliferative changes and irregular menstrual bleeding.[15] In contrast, Amooee et al reported menstrual irregularities in only 14.4% of women with PCOS and none among those with unexplained infertility. This discrepancy may be attributed to the stringent inclusion criteria of their study, which limited participants to those with normal endometrial thickness on ultrasonography, thereby reducing the potential for endometrial hyperplasia and its contribution to menstrual dysfunction. Clinical features of hyperandrogenism, including acne and hirsutism, were significantly more prevalent in obese women with polycystic ovary syndrome (PCOS) compared to those without PCOS (p<0.001), consistent with the findings of Saxena et al.[16] The underlying pathophysiology involves hyperinsulinemia and elevated luteinizing hormone (LH) levels in women with PCOS, which stimulate ovarian theca cells to produce increased amounts of androstenedione. Additionally, hyperinsulinemia suppresses the synthesis of sex hormone-binding globulin (SHBG), leading to elevated circulating free testosterone levels.[17]

The prevalence of impaired glucose tolerance and diabetes was higher among women with PCOS compared to unexplained group (p=0.002), which was consistent with studies by Amooee et al, Al-Jefout et al and Indhavivadhana et al.[6,9,11] PCOS is associated with hyperandrogenism and insulin resistance leading to higher prevalence of diabetes in these women. There was higher prevalence of hypertension in PCOS group which was similar to studies by Shi et al, Hachmi et al and Ozkan et al.[18-20] Women with PCOS are at high risk of hypertension due to obesity, insulin resistance, atherogenic dyslipidaemia and metabolic syndrome predisposing to development of early atherosclerosis and cardiovascular morbidity.

In our study the mean levels of FSH, Prolactin, and TSH were comparable between the groups, which was similar to the studies done by Hepsen et al and Al-Saab et al.[21,22] The LH and testosterone levels were found to be significantly higher in women with PCOS compared to women without PCOS features (p=0.017, p<0.001) similar to studies by Amooee et al Kumar et al and Hafed et al.[9,22,23] In PCOS, there is an increase in the pulsatile release of gonadotropin-releasing hormone (GnRH), which leads to a disproportionate elevation in luteinizing hormone (LH) relative to follicle-stimulating hormone (FSH). The resulting elevated LH levels stimulate theca cells to produce excessive androgens, contributing to theca cell hyperplasia, increased follicular count, and clinical manifestations of hyperandrogenism. These include polycystic ovarian morphology, chronic anovulation, hirsutism, androgenic alopecia, and insulin resistance. Elevated serum testosterone in PCOS is attributed to both increased androgen production and hyperinsulinemia. Insulin resistance, commonly observed in PCOS, induces compensatory hyperinsulinemia, which suppresses hepatic synthesis of sex hormone-binding globulin (SHBG), thereby increasing free circulating androgen levels and exacerbating the clinical features of hyperandrogenism.

Ultrasound parameters like endometrial thickness and ovarian volume were significantly higher in PCOS women compared to unexplained infertility group (p=0.001), which was similar to studies by Indhavivadhana et al, Panchal et al.[11,24] The reason for increased endometrial thickness in these women is chronic anovulation leading to hyperoestrogenism unopposed by progesterone and increased LH levels causing more proliferative endometrial growth and subsequent endometrial hyperplasia and cancer. In a study by Cheung et al, an endometrial thickness cut-off of 7 mm was suggested for predicting endometrial hyperplasia.[25]

Later a study by McCormick et al found a higher endometrial thickness cut-off of 9.3 mm with superior specificity and positive predictive value.[26] Hyperandrogenism, hyperestrogenism and decreased oocyte secreting growth factors leads to excess number of small follicles and arrest of follicular growth causing increased ovarian volume in women with PCOS.[27]

Patients with normal transvaginal ultrasonography may have a 20-40% prevalence of mild intrauterine diseases during hysteroscopy.[9,16] Majority of patients in our study had normal hysteroscopy findings which was consistent with studies.[28] In a large retrospective research including 1500 women who had diagnostic hysteroscopy, Garuti and colleagues found that hysteroscopy had the best sensitivity and specificity for diagnosing endometrial polyps and the lowest for diagnosing endometrial hyperplasia.[29] In the PCOS group, 82% of women demonstrated normal hysteroscopic findings, while the remaining exhibited hyperplastic endometrium (3.5%), hyperemic endometrium (8.2%), and endometrial micropolyps (5.8%). In comparison, 70% of women with unexplained infertility had normal hysteroscopy, with the most frequently observed abnormalities being uterine polyps (8.1%), intrauterine adhesions (9.9%), and a sub-septate uterus (9.3%).

These findings are consistent with previous literature reporting a high prevalence of normal endometrial morphology in PCOS patients on hysteroscopy. Shokeir et al observed normal endometrial patterns in 75% of PCOS patients undergoing hysteroscopy, with hyperplastic changes identified in approximately 6% of cases, often attributed to prolonged unopposed estrogen exposure due to chronic anovulation.[30] Similarly, Tsuji et al documented that PCOS patients may exhibit subtle endometrial

changes like focal hyperemia or micropolyps, which could represent subclinical inflammation or early endometrial dysfunction, potentially affecting implantation.[31]

In the unexplained infertility group, the prevalence of uterine abnormalities was higher. This aligns with findings by Cenksoy et al who reported intrauterine adhesions and endometrial polyps as common incidental findings during diagnostic hysteroscopy in unexplained infertility cases, often missed on transvaginal sonography or HSG.[32] Pundir and El Toukhy's meta-analysis further reinforces the role of hysteroscopy in improving pregnancy outcomes in women with unexplained infertility by detecting and treating intrauterine pathologies that may not be evident through non-invasive imaging techniques.[33]

The identification of a sub-septate uterus in 9.3% of unexplained infertility cases is significant. Septate anomalies are known to be associated with impaired implantation and increased miscarriage risk. Their correction via hysteroscopic metroplasty has been shown to improve reproductive outcomes, as demonstrated by Valle and Ekpo.[34]

Endometrial integrity plays a crucial role in female fertility, making the evaluation of endometrial histology an important component in assessing women with PCOS.[35]

In this study, we investigated women with normal endometrial thickness on transvaginal ultrasonography and performed hysteroscopic endometrial biopsies, which showed different frequencies of endometrial lesions between the PCOS and UI groups: proliferative endometrium (48%), disordered proliferative (17.6%), endometrial polyp (5%), and secretory endometrium (16%) in the PCOS group, while the most common histological findings included secretory endometrium (56%), proliferative endometrium (27%) and endometrial polyp 8%%) in the UI group, with no disordered proliferative endometrium. Endometrial hyperplasia was detected in 7 patients (5.5%) in women with PCOS compared to none in UI group. Disordered proliferative endometrium is abnormal proliferative endometrium with architectural changes due to persistent unopposed estrogen stimulation, considered benign, not precancerous.[36,37] Unopposed estrogen on disordered proliferative endometrium in the early phase can later develop into hyperplasia.

Amooee et al similarly reported that 17.1% of infertile women with PCOS exhibited disordered proliferative endometrium despite having normal endometrial thickness on ultrasound and no abnormalities on hysteroscopy, consistent with the findings of our study.[9] They further demonstrated a lack of correlation between hysteroscopic impressions and histopathological outcomes (p=0.28, contingency coefficient=0.3). These observations underscore the need to evaluate endometrial abnormalities beyond their association with endometrial thickness alone.

In a large retrospective analysis of 1,500 women undergoing diagnostic hysteroscopy, Garuti and colleagues correlated hysteroscopic findings with histological diagnoses and reported cases of endometritis, endometrial polyps, endometrial hyperplasia, and endometrial malignancies in 21, 265, 185, and 102 patients, respectively.[29] Their study highlighted that hysteroscopy demonstrated the highest sensitivity and specificity for detecting endometrial polyps, while its diagnostic performance was poorest for endometrial hyperplasia.[38] To predict the diagnosis of hyperplasia, hysteroscopy showed an overall sensitivity, specificity, NPV, and PPV of 63.7%, 91.7%, 91.3%, and 64.7%, respectively.

Endometrial polyps are benign proliferative lesions typically detected incidentally on transvaginal ultrasonography, hysterosalpingography, or sonohysterography.[13] In contrast, endometrial micropolyps defined as small projections measuring 1–2 mm are identifiable only through hysteroscopic examination.[39] These micropolyps are strongly associated with chronic endometritis, characterized by plasma cell infiltration of the endometrial stroma, stromal edema, thickening, and periglandular hyperemia.[40] A retrospective study estimated the prevalence of endometrial micropolyps to be approximately 11% based on hysteroscopic assessment with conventional tissue staining, and further demonstrated their relationship with endometritis and infertility. The clinical relevance of chronic endometritis and micropolyps lies in both their association with infertility and their potential implications for the development and treatment of endometrial hyperplasia and endometrial cancer.[41-42]

To our knowledge, no prior studies have specifically documented the histopathological profiles of women with PCOS who exhibit normal hysteroscopic findings. Most available literature reports a strong concordance between hysteroscopic impressions and histological diagnoses for intrauterine pathologies. In contrast, our study demonstrated no significant correlation between the two modalities, indicating that a normal hysteroscopic appearance does not reliably reflect a normal endometrium. This underscores the need for histopathological assessment in women with PCOS, even when endometrial thickness is within normal limits. Although no premalignant or malignant lesions were identified in our cohort, hysteroscopy alone failed to detect endometrial polyps particularly micropolyps later identified on biopsy. This may be attributed to the absence of increased endometrial thickness (>12 mm) on transvaginal ultrasound in both groups.

This study has certain limitations. Being cross-sectional in design, long-term follow-up of participants was not feasible, which limited assessment of the true prevalence and progression of endometrial hyperplasia. The sample size was relatively small, which may have affected the generalizability of the findings. Although hysteroscopy

was performed, a more detailed and systematic hysteroscopic evaluation could have helped identify additional subtle endometrial pathologies in infertile women.

The overall prevalence of endometrial hyperplasia in the study population was low (5.5%), which limited the ability to analyse and identify predictive factors associated with its occurrence. Furthermore, the study did not assess the correlation between ultrasonographic endometrial patterns or echogenicity and histologically confirmed endometrial hyperplasia, which could have provided additional non-invasive diagnostic insights.

## CONCLUSION

This study shows that normal hysteroscopic findings may still correspond with abnormal endometrial histology in a subset of infertile women with PCOS who do not exhibit endometrial thickening. These results suggest that hysteroscopy without concurrent biopsy may miss subtle pathologies such as micropolyps. Therefore, combined hysteroscopic and histological evaluation is advisable for all women with PCOS, regardless of endometrial thickness or ultrasound findings.

*Funding: No funding sources*
*Conflict of interest: None declared*
*Ethical approval: The study was approved by the Institutional Ethics Committee*

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**Cite this article as:** Thyagaraju C, Chandrashekaran M, Badhe B, Kumar S. Endometrial hysteroscopic and histopathological characteristics in infertile women with polycystic ovary syndrome versus unexplained infertility: a comparative cross-sectional study. Int J Reprod Contracept Obstet Gynecol 2026;15:642-50.