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Correlating clinical, hysteroscopic, and histological findings in chronic pelvic inflammatory disease: diagnostic challenges and preliminary scoring system development

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ABSTRACT

Objective. Chronic pelvic inflammatory disease (CPID) encompasses various clinical presentations, notably chronic pelvic pain, infertility, abnormal uterine bleeding (AUB), and miscarriage, yet its diagnostic criteria remain elusive, leading to underdiagnosis and inadequate management. This study aimed to evaluate the correlation between clinical symptoms, hysteroscopic findings, and histopathological results in CPID, addressing diagnostic challenges and proposing a preliminary scoring system to improve patient care

Materials and Methods. We conducted a retrospective analysis of 213 women with symptoms suggestive of CPID who had undergone hysteroscopy and endometrial biopsy between October 2016 and March 2022. Data analysis included examination of clinical presentation,

hysteroscopic findings (using predefined criteria), and histopathological results (using standardized plasma cell counts). A preliminary scoring system integrating key diagnostic parameters was developed based on our findings and literature review.

Results. Among 213 patients (mean age 41.9 ± 10.8 years), hysteroscopic findings suggestive of endometritis (endometrial wall edema, micro polyps, and erythema) were observed in 126 cases (59.2%); however, histopathology-confirmed endometritis (≥ 5 plasma cells/10 HPF) was observed in only 23 cases (10.8%). Significant paired discordance was found between hysteroscopic signs and histological confirmation of endometritis (McNemar test, $p < 0.001$). Diagnostic accuracy analysis revealed area under curve (AUC) values ranging from 0.46 to 0.67 for various parameter combinations, indicating modest discrimination. Based on these findings and literature review, we developed a preliminary scoring system incorporating clinical, imaging, operative, and histopathological parameters.

Conclusions. Correlating clinical, hysteroscopic, and histological findings is essential but challenging in CPID diagnosis. The proposed preliminary scoring system offers a structured framework for CPID assessment but requires validation. Further research is warranted to validate and refine diagnostic approaches for CPID, as early recognition and intervention are paramount to mitigate adverse outcomes

Key words

Chronic pelvic inflammatory disease; chronic pelvic pain; infertility; abnormal uterine bleeding; miscarriage; hysteroscopy; endometritis

Introduction

Chronic pelvic inflammatory disease (CPID) encompasses a wide range of clinical presentations including chronic pelvic pain, infertility, abnormal uterine bleeding (AUB), and miscarriage [1]. Despite its significant impact on women's health, there is no consensus on definitive diagnostic criteria or guidelines for CPID [2]. This diagnostic uncertainty often leads to underdiagnosis and inadequate management.

CPID represents chronic inflammation of the upper genital tract, distinct from but often overlapping with chronic endometritis (CE), which specifically refers to endometrial inflammation [3]. The estimated prevalence of CPID ranges from 0.28% to 1.67% [4], but accurate diagnosis remains challenging due to variable presentations and lack of standardized criteria.

If not properly identified and treated, CPID may lead to infertility, ectopic pregnancy, chronic pelvic pain, and recurrent pelvic inflammatory disease [5]. These complications significantly affect women's health, reduce quality of life, and increase economic burden [6].

Despite the Centers for Disease Control and Prevention (CDC) publishing guidelines for PID diagnosis, the criteria's sensitivity and specificity remain relatively low [7]. There is a critical gap in understanding the correlation between clinical symptoms, hysteroscopic findings, and

histopathological results in CPID. Most studies have focused on individual diagnostic modalities rather than their combined utility.

This study aims to address this gap by comprehensively evaluating patients with symptoms suggestive of CPID who underwent diagnostic hysteroscopy and endometrial biopsy. Our objectives are to: (1) delineate the correlation between clinical presentation, hysteroscopic findings, and histopathological results; (2) analyze the diagnostic accuracy of different parameter combinations; and (3) propose a preliminary scoring system based on our findings to standardize CPID assessment.

Materials and Methods

Study Design and Setting:

We conducted a retrospective cohort study at Jordan University Hospital (JUH), a tertiary care center in Amman, Jordan. The study was approved by the Institutional Review Board of Jordan University Hospital (Approval No. 10/2020/1407; Date: January 1st, 2024). Due to the retrospective nature of the study using fully anonymized data, the ethical committee granted a waiver for informed consent.

Study Population:

We reviewed medical records of all women who underwent diagnostic hysteroscopy and endometrial biopsy at JUH between October 2016 and March 2022. During this period, 387 patients underwent these procedures for various reasons. After applying exclusion criteria, 213 patients were included in the final analysis (Figure 1).

Inclusion Criteria:

1. Women aged ≥ 18 years
2. Symptoms suggestive of CPID: unexplained chronic pelvic pain (including dyspareunia and dysmenorrhea), infertility (primary or secondary), recurrent miscarriages (≥ 2), or abnormal uterine bleeding (menorrhagia, post-menopausal bleeding, perimenopausal bleeding)
3. Completion of diagnostic hysteroscopy and endometrial biopsy
4. Absence of acute genital infections or sexually transmitted infections at time of evaluation

Exclusion Criteria:

1. Pregnancy

2. Identifiable gynecological conditions explaining symptoms (fibroid uterus, endometriosis diagnosed at any stage, endometrial polyps >1cm, uterine malformations)
3. Recent antibiotic treatment (within 4 weeks before biopsy)
4. Hormonal therapy within 3 months
5. Intrauterine device in place

Hysteroscopic Procedure and Criteria:

Hysteroscopies in premenopausal women were performed during the follicular phase (days 5–12), while procedures in peri- and postmenopausal women were performed irrespective of cycle timing, by one of three experienced gynecologists using a 5mm rigid hysteroscope with normal saline distension medium. Procedures were recorded and reviewed independently by two blinded gynecologists with inter-observer agreement of 89% (Cohen's $\kappa = 0.76$).

Hysteroscopic criteria suggestive of endometritis/CPID included [8]:

1. Endometrial wall edema (diffuse or localized swelling)
2. Micropolyps (<1mm multiple polypoid projection)
3. Erythema (diffuse or patchy redness)
4. Increased vascularity (abnormal vessel pattern)
5. Strawberry appearance (focal red spots)

A finding was considered positive if at least two of these criteria were present.

Endometrial Biopsy and Histological Criteria:

Endometrial biopsies were obtained under direct hysteroscopic visualization from areas showing abnormal findings when present, or from the uterine fundus and both cornual regions when no focal abnormalities were visible. Specimens were fixed in formalin, embedded in paraffin, and stained with hematoxylin and eosin (H&E). All slides were reviewed independently by two experienced pathologists blinded to clinical and hysteroscopic findings, with disagreement resolved by consensus.

Histological diagnosis of chronic endometritis was based on the presence of plasma cells in the endometrial stroma [9]. Following recent consensus [10], we used a threshold of ≥ 5 plasma cells per 10 high-power fields (HPF, 400 \times magnification) as diagnostic. Plasma cells were counted across ten non-overlapping high-power fields selected from areas of highest inflammatory density. Interobserver agreement between pathologists was high, with discrepancies resolved by joint slide review and consensus.

Immunohistochemistry for CD138 was performed in equivocal cases.

Data Collection:

Data were collected from electronic medical records including: demographic characteristics, clinical symptoms, pelvic ultrasound findings, hysteroscopic findings, histological results, and treatment outcomes. A standardized data extraction form was used to ensure consistency.

Statistical Analysis:

Statistical analysis was performed using STATA-17 software (StataCorp, College Station, TX, USA). Descriptive statistics included means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. The chi-squared test or Fisher's exact test was used for categorical variables, and the Mann-Whitney U test for continuous variables. Diagnostic accuracy measures (sensitivity, specificity, positive predictive value [PPV], negative predictive value [NPV]) were calculated with 95% confidence intervals using histological diagnosis as reference standard. Area under receiver operating characteristic (ROC) curves (AUC) were calculated for various parameter combinations. A p-value <0.05 was considered statistically significant.

Scoring System Development:

The preliminary scoring system was developed through: (1) review of existing literature on CPID/CE diagnostic criteria; (2) analysis of associations between variables and histological diagnosis in our cohort; (3) expert consensus among authors regarding clinical relevance. Points were assigned based on reported diagnostic value in literature and prevalence in our cohort. No formal regression modeling was performed due to sample size limitations; therefore, the scoring system is presented strictly as a hypothesis-generating framework rather than a validated diagnostic tool.

Sample Size Justification:

Based on estimated CPID prevalence of 1.67% in symptomatic women[4] and expecting 20% histological confirmation rate, a sample of 200 patients provides 80% power to detect correlations with effect size ≥ 0.2 at $\alpha=0.05$.

Results

Patient Characteristics:

A total of 213 patients met inclusion criteria (Figure 1). Baseline characteristics are presented in Table 1. The mean age was 41.9 years (SD \pm 10.8, range 21-82 years), with mean parity of 3.23 (SD \pm 2.41) and mean number of miscarriages of 1.7 (SD \pm 2.29).

Of the total cohort, 47 patients (22.1%) were peri- or postmenopausal at the time of hysteroscopy.

Hysteroscopic and Histological Findings:

Hysteroscopic findings are summarized in Table 2. Findings suggestive of endometritis were observed in 126 patients (59.2%), with micropolyps (41.3%) and erythema (38.5%) being most common. Adhesions were observed in 31 patients (14.5%).

Histopathological examination confirmed chronic endometritis in 23 patients (10.8%, 95% CI: 7.0-15.8%). Among these, plasma cell counts ranged from 5-42 per 10 HPF (median: 8). CD138 immunohistochemistry was performed in 15 cases with equivocal H&E findings, confirming diagnosis in 9 cases.

Findings by Clinical Presentation:

Table 3 presents hysteroscopic and histological findings stratified by primary presenting symptom. Among patients with AUB (n=137), 86 (62.8%) had hysteroscopic findings suggestive of endometritis, while only 15 (11.0%) had histological confirmation. Similar discordance patterns were observed across other symptom groups.

We observed significant associations between parity >2 and clinical indication (p=0.001), and between clinical indication and hysteroscopic findings (p=0.013). However, no significant association was found between clinical indication and histological findings (chi-square test, p=0.42), nor between hysteroscopic and histological findings (chi-square test, p=0.38), indicating poor agreement despite significant paired discordance.

Agreement analysis demonstrated low concordance between hysteroscopic and histological findings (Cohen's $\kappa = 0.12$), confirming that statistically significant paired discordance does not imply diagnostic agreement.

Diagnostic Accuracy Analysis:

Table 4 presents diagnostic accuracy measures for non-histological predictors against histological diagnosis as the reference standard; combinations incorporating histology are shown for exploratory comparison only. The combination of clinical indications with hysteroscopic findings showed high sensitivity (100%) but low specificity (34.2%), while combinations including histological parameters showed higher specificity but lower sensitivity. All AUC values were below 0.70, indicating modest discrimination.

Preliminary Scoring System:

Based on our findings and literature review, we developed a preliminary CPID scoring system (Table 5). The system incorporates clinical symptoms (8 points), demographic factors (7 points), hysteroscopic findings (5 points), histological findings (2 points), and ultrasound findings (3 points), for a maximum of 25 points. Higher scores suggest greater likelihood of CPID. The scoring system is conceptualized as a two-stage framework, comprising a pre-test clinical-hysteroscopic assessment followed by post-test histological confirmation.

Discussion

This study highlights the diagnostic challenges in CPID, revealing significant discordance between hysteroscopic findings and histopathological confirmation. While 59.2% of patients had hysteroscopic signs suggestive of endometritis, only 10.8% had histological confirmation using current consensus criteria (≥ 5 plasma cells/10 HPF). This discrepancy aligns with recent literature suggesting that hysteroscopy may have high sensitivity but limited specificity for CPID diagnosis [11].

The modest diagnostic accuracy measures (AUC values 0.46-0.67) underscore the complexity of CPID diagnosis. Our findings suggest that while hysteroscopy is valuable for detecting endometrial abnormalities, it should not replace histological examination. The high NPV (93.5%) of combined hysteroscopic and histological findings suggests this combination may be useful for ruling out CPID when both are negative.

Several factors may explain the observed discordance: (1) **Focal nature of inflammation:** Endometrial inflammation in CPID may be patchy, leading to sampling error [12]; (2) **Timing of biopsy:** Although performed in follicular phase, inflammation may vary cyclically [13]; (3) **Threshold variability:** The optimal plasma cell threshold for CPID diagnosis remains debated [14]; (4) **Spectrum of disease:** Some hysteroscopic findings may represent non-specific inflammatory changes rather than true chronic endometritis.

Our patient population (mean age 41.9 years) differs from typical CPID cohorts, which often focus on younger women. This may reflect referral patterns at our tertiary center or differing CPID manifestations across age groups. The high parity (mean 3.23) and miscarriage rate (mean 1.7) in our cohort align with Jordan's demographic profile [15] and suggest possible associations between reproductive history and CPID risk.

The proposed preliminary scoring system represents an initial attempt to standardize CPID assessment by integrating multiple diagnostic parameters. The point assignments were based on literature review and prevalence in our cohort, with higher points for parameters showing stronger associations with histological diagnosis. Importantly, we acknowledge this system requires validation before clinical implementation. History of PID and recent IUD use were retained based on consistent associations reported in prior literature, although their individual associations with histology did not reach statistical significance in this cohort.

Inclusion of histological findings reflects post-test confirmation rather than pre-biopsy triage, and score weights should be interpreted cautiously.

Strengths of our study include comprehensive evaluation of multiple diagnostic modalities, standardized histological criteria, and detailed diagnostic accuracy analysis. However, several limitations must be acknowledged: (1) **Retrospective design** with inherent selection bias; (2) **Single-center study** limiting generalizability; (3) **Lack of standardized hysteroscopic criteria** in literature; (4) **No microbiological correlation**; (5) **Small sample size** for some subgroups; (6) **Preliminary nature of scoring system** without validation.

Future research should focus on: (1) Prospective validation of diagnostic criteria; (2) Multicenter studies to establish generalizable standards; (3) Correlation with microbiological findings; (4) Development of evidence-based scoring systems through regression modeling; (5) Evaluation of treatment response based on different diagnostic combinations.

Conclusions

This study demonstrates significant discordance between hysteroscopic findings and histopathological confirmation in CPID, highlighting ongoing diagnostic challenges. While hysteroscopy shows high sensitivity for detecting endometrial abnormalities, it should be interpreted alongside histological examination. The proposed preliminary scoring system provides a structured framework for CPID assessment but requires prospective validation. Future studies should focus on standardizing diagnostic criteria and developing validated algorithms to improve CPID diagnosis and management.

COMPLIANCE WITH ETHICAL STANDARDS

Authors' contribution

O.A-K.: Conceptualization, Project administration, Writing -- original draft, Writing -- review & editing

L.AK.: Data curation, Writing -- review & editing

L.M.A-M.: Writing -- original draft, Writing -- review & editing, Formal Analysis, Supervision, Validation

R.H.: Data curation

R.A.S.: Data curation

O.AK: Data collection

K.AQ: Data collection

N.A.A-H.: Writing -- review & editing

N.A.S.: Investigation

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Study registration

Not applicable.

Disclosure of interests

The authors have no relevant financial or non-financial interests to disclose.

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Institutional Review Board of Jordan University Hospital/Medical school (Date:

January 1st 2024; Approval No. 10/2020/1407). Retrospective analysis of existing anonymized data was permitted under local regulations.

Informed consent

Not applicable due to the retrospective nature of the study and the use of fully anonymized clinical data. The ethical committee granted a waiver for informed consent.

Data sharing:

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Table 1. Baseline Characteristics of Study Population (n=213)

Characteristic	Mean \pm SD or n (%)	Range
Age (years)	41.9 \pm 10.8	21-82
Parity	3.23 \pm 2.41	0-11
Miscarriages	1.70 \pm 2.29	0-9
Presenting Symptoms		
Abnormal uterine bleeding	137 (64.3%)	
Infertility	27 (12.7%)	
Recurrent miscarriage	42 (19.7%)	
Chronic pelvic pain	8 (3.7%)	
Mixed complaints*	42 (19.7%)	
* *Patients could report multiple symptoms; for subsequent analyses, a single primary presenting symptom was assigned based on the main indication for hysteroscopy.		

Table 2. Hysteroscopic Findings (n=213)

Finding	n (%)	95% CI
Any findings suggestive of endometritis	126 (59.2%)	52.3-65.8%
Micropolyps	88 (41.3%)	34.7-48.2%
Erythema	82 (38.5%)	32.0-45.3%
Endometrial edema	64 (30.0%)	24.0-36.7%
Increased vascularity	52 (24.4%)	18.9-30.7%
Strawberry appearance	38 (17.8%)	13.0-23.6%
Adhesions	31 (14.5%)	10.1-20.0%

Finding	n (%)	95% CI
Normal hysteroscopy	87 (40.8%)	34.2-47.7%

Table 3. Findings by Assigned Primary Presenting Symptom

Symptom	N	Hysteroscopic Findings Suggestive of Endometritis n (%)	Histologically Confirmed Endometritis n (%)
Abnormal uterine bleeding	137	86 (62.8%)	15 (11.0%)
Infertility	27	14 (51.9%)	3 (11.1%)
Recurrent miscarriage	42	23 (54.8%)	5 (11.9%)
Chronic pelvic pain	8	3 (37.5%)	0 (0%)

Table 4. Diagnostic Accuracy of Parameter Combinations*

Combination	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)
Clinical indications† + Hysteroscopic findings‡	100% (85.1-100%)	34.2% (27.4-41.5%)	17.5% (12.0-24.3%)	100% (94.3-100%)	0.67 (0.60-0.74)

Combination	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)
Clinical indications + Histological findings	91.3% (73.2- 97.6%)	8.9% (5.3- 14.2%)	11.1% (7.5- 15.9%)	90.0% (68.3- 97.1%)	0.50 (0.43- 0.57)
Hysteroscopic findings + Histological findings	60.9% (40.8- 77.8%)	67.9% (60.7- 74.4%)	18.6% (11.6- 28.2%)	93.5% (88.3- 96.5%)	0.64 (0.57- 0.71)
Infertility + Hysteroscopic findings	13.0% (3.7- 32.1%)	89.5% (84.2- 93.2%)	13.0% (3.7- 32.1%)	89.5% (84.2- 93.2%)	0.51 (0.44- 0.58)
AUB + Hysteroscopic findings	65.2% (44.9- 81.2%)	38.4% (31.4- 45.9%)	11.6% (7.1- 18.2%)	89.6% (81.5- 94.4%)	0.52 (0.45- 0.59)

*Using histological diagnosis (≥ 5 plasma cells/10 HPF) as reference standard

†Clinical indications: AUB, infertility, recurrent miscarriage, or chronic pelvic pain ‡Hysteroscopic findings: ≥ 2 of: micropolyps, erythema, edema, increased vascularity, strawberry appearance

Combinations including histological findings are presented for exploratory comparison only and do not represent independent diagnostic tests, as histology remains the reference standard.

Table 5. Preliminary CPID Scoring System

Category	Parameter	Points
Clinical Symptoms		8

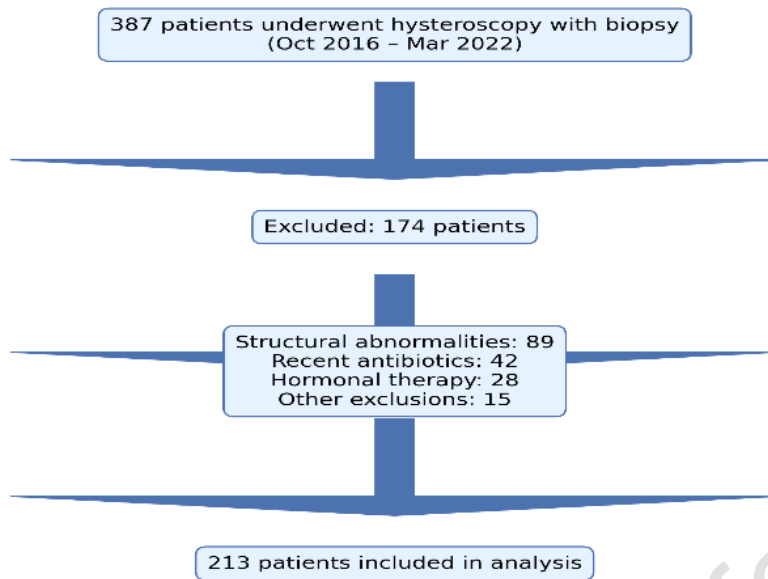
Category	Parameter	Points
	Chronic pelvic pain (>6 months)	2
	Abnormal uterine bleeding	2
	Infertility (unexplained)	2
	Recurrent miscarriage (≥ 2)	2
Demographics		7
	Age <35 years	1
	Parity >2	2
	History of PID	2
	Recent IUD use	2
Hysteroscopic Findings		5
	Micropolyps	1
	Erythema	1
	Endometrial edema	1
	Increased vascularity	1
	Strawberry appearance	1

Category	Parameter	Points
Histological Findings		2
	≥5 plasma cells/10 HPF	2
Ultrasound Findings		3
	Endometrial thickness >10mm (follicular)	1
	Heterogeneous endometrium	1
	Fluid in endometrial cavity	1
Total Possible Score		25

Table 6. Score Distribution in Study Population

Score Range	n (%)	Histological Endometritis in Range n (%)
0-5	34 (16.0%)	0 (0%)
6-10	89 (41.8%)	3 (3.4%)
11-15	67 (31.5%)	12 (17.9%)
16-20	19 (8.9%)	7 (36.8%)
21-25	4 (1.9%)	1 (25.0%)

Figure 1. Study Flow Diagram



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