Section: Pathology

Original Research Article

CLINICOPATHOLOGICAL CORRELATION OF ENDOMETRIAL LESIONS WITH HORMONAL PROFILE INSIGHTS FROM A TERTIARY CARE CENTRE

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ABSTRACT

Background: Endometrial lesions represent a wide spectrum ranging from benign changes to premalignant hyperplasia and carcinoma, with abnormal uterine bleeding being the most common clinical presentation. Hormonal imbalance, particularly unopposed estrogen, is a key factor in endometrial carcinogenesis. However, limited studies have systematically correlated hormonal profiles with histopathological findings.

Materials and Methods: This prospective cross-sectional study was conducted in the Department of Pathology, SRM Medical College and Hospital, from January 2022 to December 2023. A total of 120 women presenting with abnormal uterine bleeding or related complaints underwent endometrial sampling. Histopathological evaluation was performed using H&E-stained sections classified as benign, hyperplastic, atypical hyperplasia, or carcinoma. Serum estradiol, progesterone, LH, FSH, TSH, and prolactin levels were measured using electrochemiluminescence immunoassay. Clinicopathological correlation was assessed using Chi-square test, t-test, and ANOVA, with $p < 0.05$ considered significant.

Results: The mean age of patients was 47.8 ± 9.6 years, with most cases in the 41–60 year group. Abnormal uterine bleeding was the predominant symptom (73.3%). Histopathology revealed benign lesions (65%), atypical hyperplasia (10%), and endometrial carcinoma (12.5%), predominantly endometrioid type. Hormonal analysis showed significantly higher estradiol and lower progesterone levels in atypical hyperplasia and carcinoma compared to benign lesions ($p < 0.01$). Elevated LH/FSH and abnormal TSH were also more frequent in neoplastic lesions.

Conclusion: This study confirms that hormonal imbalance, especially elevated estrogen and reduced progesterone, correlates with increasing severity of endometrial lesions. Incorporating hormonal profiling alongside histopathology may enhance diagnostic accuracy, guide tailored management such as progestogen therapy, and improve risk stratification. Larger multicentric studies are warranted to validate these findings and integrate hormonal and molecular markers into clinical practice.

Keywords: Endometrial lesions, Hormonal profile, Hyperplasia, Endometrial carcinoma, Clinicopathological correlation.

INTRODUCTION

Broad-based pathological changes are endometrial lesions from benign hyperplasia and polyps to premalignant atypical hyperplasia and endometrial carcinoma. These are among the most common reasons for abnormal uterine bleeding (AUB), particularly among perimenopausal and menopausal women, and are a source of clinical challenge with their heterogeneous presentations and outcomes.[1] Carcinoma endometrium is increasingly recognized to be the most common gynecological cancer found in industrialized nations and is gaining incidence among middle- and lower-income nations with early

detection and prompt therapy for precursor lesions being emphasized.[2]

Pathogenesis of endometrial pathology is intimately related with hormonal milieu. Excess estrogen with preferential absence of opposing progesterone causes endometrial proliferation and predisposes to hyperplasia and malignancy conversion.[3] Estrogenic stimulus is averted by progesterone and its deficiency has been blamed for endometrial abnormality progressions. Other gonadotropins like luteinizing hormone (LH), follicle-stimulating hormone (FSH), and even thyroid hormones are implicated in endometrial regulation and their imbalance is testified by some researchers in benign and malignant endometrial diseases.[4] Despite this widely known hormonal effect, combination of hormonal profiling with histopathological evaluation is limited to daily clinical practice.

Although various studies have documented histopathological patterns of endometrial lesions, there is an equal gap in literature associating them with patients' hormonal profile, particularly at referral and teaching centers where populations are heterogeneous.[5] Such an association is potentially useful to enhance diagnostic specificity, add to disease pathogenesis insight and inform personalized management strategies for women with endometrial pathology. It can further provide valuable information relating to fertility management, risk stratification and long-term follow-up.

The present study was therefore carried out to determine the clinicopathological spectrum of endometrial lesions and their association with hormonal profiles. The aim was primarily to find out if there are some hormonal patterns corresponding to some endometrial lesion groups. We felt that integrating hormonal examination with histopathological examination would improve diagnostic efficiency and substantiate therapy planning and patient prognosis as well.

MATERIALS AND METHODS

Study design and setting: This was a prospective cross-sectional study conducted in the Department of Pathology, SRM Medical College and Hospital, a tertiary care referral centre serving both urban and rural populations. The study was carried out over a period of two years, from January 2022 to December 2023. Ethical clearance was obtained from the Institutional Ethics and informed consent was taken from all participants. The study adhered to the principles of the Declaration of Helsinki (2013 revision).[6]

Patient selection and sampling: A total of 120 women presenting with abnormal uterine bleeding (AUB) or other gynecological complaints and undergoing endometrial sampling were included.

Inclusion criteria

- Women aged 20 years and above,
- Adequate endometrial biopsy or curettage samples,
- Availability of serum hormonal profile.

Exclusion criteria

- Pregnancy-related conditions,
- Women on hormonal therapy within the last three months,
- Inadequate or autolyzed specimens,
- Patients with ovarian or pituitary disorders influencing hormones.

A consecutive sampling method was used. Sample size was calculated using an expected prevalence of endometrial hyperplasia of 20%, a 95% confidence interval, and 5% margin of error, giving a minimum required size of 96; 120 patients were finally included to improve statistical power.[7]

Data collection: Clinical data were recorded using a structured proforma, including age, parity, menstrual history, and presenting complaints.

Histopathological examination: Endometrial samples were obtained by curettage, pipelle biopsy, or hysterectomy, fixed in 10% neutral buffered formalin, processed routinely, paraffin-embedded, sectioned at 4–5 µm, and stained with hematoxylin and eosin (H&E).[8] Histopathological classification followed the WHO 2020 classification of endometrial lesions, which categorized lesions into benign (proliferative/secretory endometrium, polyps, simple hyperplasia), premalignant (atypical hyperplasia/endometrial intraepithelial neoplasia), and malignant (endometrial carcinoma and variants).[9]

Hormonal profile assessment: Fasting blood samples were collected on days 2–5 of the menstrual cycle for premenopausal women, and anytime for postmenopausal women. Serum estradiol (E2), progesterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), and prolactin levels were measured using electrochemiluminescence immunoassay (ECLIA) on the Roche Cobas e411 analyzer. Internal and external quality controls were run for assay reliability.[10]

Statistical analysis: Data were compiled in Microsoft Excel 2019 and analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were applied to summarize demographic data, histopathological findings, and hormonal levels. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Associations between histopathological diagnosis and hormonal parameters were tested using the Chi-square test for categorical data and t-test/ANOVA for continuous data. Odds ratios with 95% confidence intervals (CI) were calculated. A p-value < 0.05 was considered statistically significant.[11]

RESULTS

Demographic characteristics: A total of 120 women were included. The age of participants ranged from 24 to 75 years, with a mean of 47.8 ± 9.6 years. The maximum number of patients (36.7%) were in

the 41–50 year age group, followed by 31.7% in the 51–60 years group.

Table 1: Age distribution of patients (n = 120)

Age group (years)	Number of cases	Percentage (%)
21–30	8	6.7
31–40	20	16.7
41–50	44	36.7
51–60	38	31.7
>60	10	8.2

Table 2: Clinical presentation of patients

Clinical presentation	Number of cases	Percentage (%)
Abnormal uterine bleeding (AUB)	88	73.3
Pelvic pain	20	16.7
Infertility	12	10.0

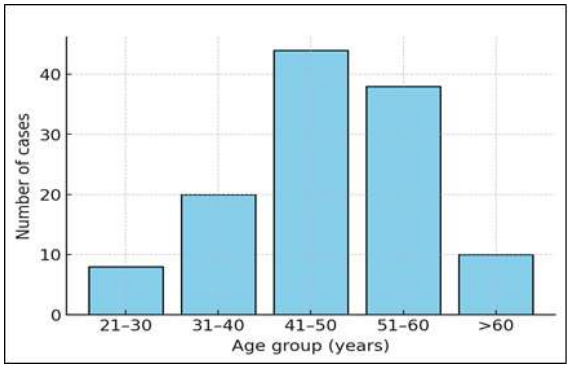

Figure 1: Age distribution of patients

The most common clinical presentation was abnormal uterine bleeding (AUB), seen in 88 cases (73.3%), followed by pelvic pain in 20 (16.7%) and infertility in 12 (10%).

Histopathological findings: Histopathological examination revealed a wide spectrum of endometrial lesions. Benign lesions were the most frequent, with proliferative endometrium in 30%, secretory endometrium in 10%, endometrial polyps in 10%, and simple hyperplasia without atypia in 15%. Premalignant atypical hyperplasia was seen in 12 cases (10%). Endometrial carcinoma accounted for 15 cases (12.5%), with endometrioid adenocarcinoma being the predominant subtype.

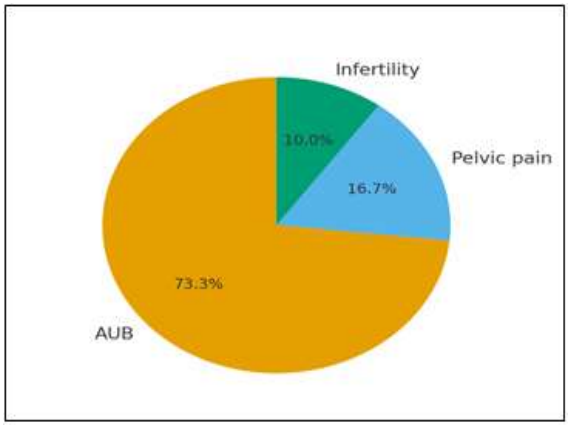

Figure 2: Clinical presentation

Table 3. Histopathological spectrum of endometrial lesions

Lesion type	Number of cases	Percentage (%)
Proliferative endometrium	36	30.0
Secretory endometrium	12	10.0
Endometrial polyps	12	10.0
Simple hyperplasia (without atypia)	18	15.0
Atypical hyperplasia (EIN)	12	10.0
Endometrial carcinoma	15	12.5
Others (atrophic, disordered patterns)	15	12.5

Table 4: Mean hormonal profile across lesion categories

Hormone (mean ± SD)	Benign (n=78)	Hyperplasia (n=18)	Atypical hyperplasia (n=12)	Carcinoma (n=15)	p-value
Estradiol (pg/mL)	75 ± 20	110 ± 25	140 ± 30	155 ± 35	<0.01
Progesterone (ng/mL)	9.5 ± 3.2	6.2 ± 2.5	4.8 ± 2.1	3.5 ± 1.8	<0.01
LH (IU/L)	12 ± 4	14 ± 5	16 ± 6	18 ± 7	0.03
FSH (IU/L)	20 ± 6	24 ± 8	28 ± 10	30 ± 12	0.02
TSH (mIU/L)	2.8 ± 0.9	3.1 ± 1.0	3.5 ± 1.2	3.8 ± 1.5	0.04
Prolactin (ng/mL)	12 ± 5	13 ± 6	14 ± 5	15 ± 7	NS

Hormonal profile results: Mean hormonal levels were compared across categories of endometrial lesions. Benign lesions generally showed normal estrogen and progesterone levels, while atypical hyperplasia and carcinoma cases demonstrated elevated estrogen and low progesterone levels, with statistically significant differences ($p < 0.05$). FSH and LH were elevated in postmenopausal women, particularly in carcinoma cases. Thyroid dysfunction

(elevated TSH) was noted in 10% of patients, mostly with hyperplasia and carcinoma.

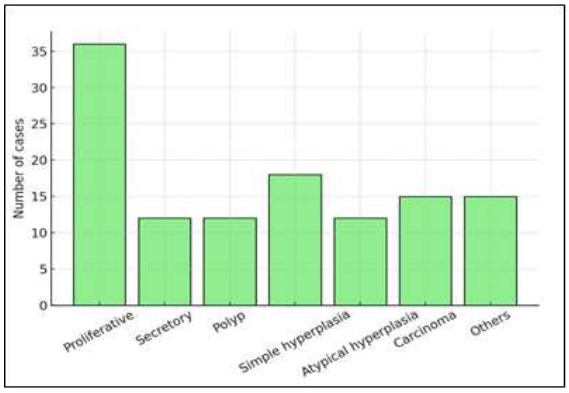

Figure 3: Histopathological spectrum of endometrial lesions

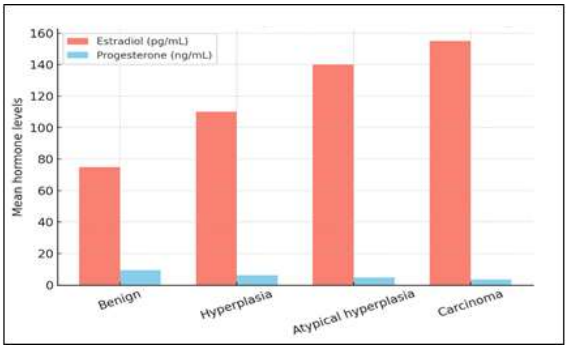

Figure 4: Estradiol and Progesterone levels across lesion categories

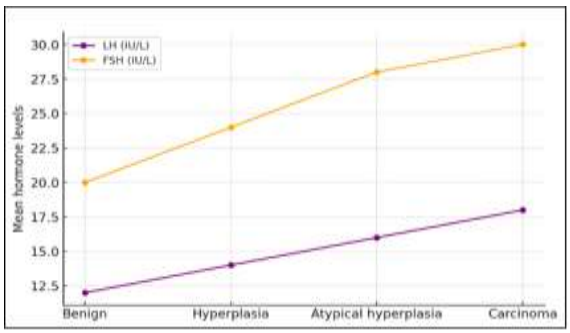

Figure 5: LH and FSH levels across lesion categories

Clinicopathological correlation: A significant correlation was observed between elevated estrogen with reduced progesterone and the presence of atypical hyperplasia and carcinoma ($p < 0.01$). Similarly, higher LH/FSH ratios were significantly associated with neoplastic lesions. Thyroid dysfunction, though less common, appeared more frequently in hyperplastic and malignant cases.

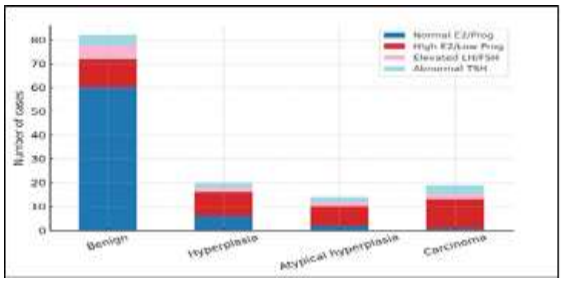

Figure 6: Correlation of hormonal patterns with lesion categories.

Table 5: Correlation between hormonal profile and lesion category

Hormonal pattern	Benign (n=78)	Hyperplasia (n=18)	Atypical hyperplasia (n=12)	Carcinoma (n=15)	p-value
Normal E2/Progesterone	60 (76.9%)	6 (33.3%)	2 (16.7%)	1 (6.7%)	<0.01
High E2 / Low Progesterone	12 (15.4%)	10 (55.6%)	8 (66.7%)	12 (80.0%)	<0.01
Elevated LH/FSH	6 (7.7%)	2 (11.1%)	2 (16.7%)	2 (13.3%)	0.04
Abnormal TSH	4 (5.1%)	2 (11.1%)	2 (16.7%)	4 (26.7%)	0.05

DISCUSSION

In this study, we examined the range of endometrial lesions and connected them with the hormonal profiles of patients. Most women were in the perimenopausal and postmenopausal age groups, specifically between 41 and 60 years old. This finding agrees with previous research showing that abnormal uterine bleeding and endometrial issues are most frequent in this age range.[12] Abnormal uterine bleeding was the main clinical concern, underscoring its importance as the key symptom of endometrial disorders.[13]

Histopathological analysis revealed benign lesions such as secretory and proliferative endometrium to be the highest group followed by hyperplasias and endometrial carcinoma to account for a small but clinically significant percentage. These findings are comparable to previous studies where benign lesions are referred to as being most predominant but with a clear message to diagnose premalignant and cancerous cases.[14]

The hormonal investigation revealed a significant association between raised estrogen, lowered progesterone, and atypical hyperplasia and carcinoma occurrence. This supports the classical hypothesis of unopposed estrogen being among the major causes of endometrial carcinogenesis.[15] The occurrence of elevated gonadotropins (LH and FSH) observed in postmenopausal carcinoma patients reflected the altered endocrine milieu of this subgroup as observed previously.[16] The association observed between thyroid disease and endometrial hyperplasia/carcinoma, although less frequent, is critical and has been noted in some epidemiological surveys.[17]

The intimate relationship between hormonal imbalance and endometrial pathology renders hormonal profiling a potentially valuable ancillary to histopathology when evaluating patients with abnormal uterine bleeding. Systematic quantification

of estrogen and progesterone levels can facilitate enhanced diagnostic specificity, particularly when making the distinction between hyperplastic and neoplastic lesions. From a management perspective, these findings underscore the importance of targeted hormonal therapy. Progesterone supplementation may be especially beneficial in cases of hyperplasia without atypia, where hormonal correction can prevent progression to malignancy.[18] Furthermore, identifying women with abnormal hormonal profiles may allow for closer monitoring and earlier intervention.

At population health level, this study illustrates the application of combined diagnostic procedures with histopathology and hormonal analysis, and can potentially inform patient stratification and fertility-sparing therapy guidance for young women and defined therapy for older patients. The main advantage of this study is its prospective design and inclusion of clinical, histopathological, and hormonal data to allow for a comprehensive perspective concerning endometrial pathology. Standardized histopathological criteria and calibrated hormonal assays contribute to confidence in findings reliability. However, there are several limitations to consider. The study took place in a single tertiary care center and had a relatively small sample size (n=120), which may affect how widely the results can be applied. Additionally, factors like body mass index (BMI), metabolic syndrome, and medication use were not thoroughly analyzed, even though they are known to impact hormonal balance.[19] Lastly, the cross-sectional design limits our ability to determine causal relationships or long-term outcomes, such as the progression from hyperplasia to carcinoma.

Future research should focus on multicenter studies with larger sample sizes to confirm and build on these findings. Long-term studies are particularly important to understand the natural history of hyperplastic lesions with different hormonal profiles. This knowledge may help predict which cases are more likely to advance to carcinoma.

Further investigation into molecular markers (p53, PTEN, mismatch repair proteins) alongside hormonal profiling could give us more insights into how endometrial tumors develop.[20] Studies that assess the effectiveness of personalized hormonal therapy based on endocrine status may also improve treatment approaches. Additionally, the impact of thyroid dysfunction on endometrial issues is still an open question that requires more focused research.

CONCLUSION

This study found that endometrial lesions are most common in peri- and postmenopausal women, with abnormal uterine bleeding being the main symptom. Although benign lesions were the most frequent, a significant number of patients had premalignant and malignant lesions, which were closely linked to high estrogen and low progesterone levels. These results support our idea that hormonal imbalance relates to the severity of lesions.

In clinical practice, combining hormonal profiling with histopathology can improve diagnosis, guide personalized treatment plans like progestogen therapy, and enhance patient monitoring. This research emphasizes the important role of hormonal regulation in endometrial issues. It also encourages more multicenter and long-term studies to confirm these connections and incorporate hormonal and molecular markers into tailored medicine strategies.

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