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HISTOMORPHOLOGICAL AND IMMUNOHISTOCHEMICAL EVALUATION OF ESTROGEN AND PROGESTERONE RECEPTORS IN ENDOMETRIUM OF ABNORMAL UTERINE BLEEDING PATIENTS

Pathology

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is a common condition influenced by hormonal imbalances and structural uterine abnormalities. Assessing endometrial estrogen and progesterone receptor expression helps understand its pathogenesis and guides targeted management. **Aim:** To evaluate the histomorphology and ER/PR receptor status of the endometrium in abnormal uterine bleeding patients and correlate these findings. The study also aims to classify AUB causes and compare results with existing literature. **Material and Methods:** This prospective study on 150 AUB patients was conducted at J.L.N. Medical College, Ajmer, in 2023 using histopathology and immunohistochemistry. ER and PR expression was assessed by Allred scoring, with statistical analysis performed using the chi-square test. **Results:** The study found that AUB was most common in women aged 41–50 years, with menorrhagia as the predominant bleeding pattern and proliferative endometrium as the most frequent histology. ER and PR positivity was observed in 82.67% of cases, suggesting a strong hormonal influence. **Conclusion:** Abnormal uterine bleeding was most common in women aged 41–50 years, with menorrhagia as the leading pattern and proliferative endometrium as the predominant histology. Estrogen and progesterone receptor positivity in 83.33% of cases highlights a strong hormonal influence. Hormone receptor assessment proves valuable in diagnosing and guiding targeted management of AUB.

KEYWORDS

Abnormal uterine bleeding (AUB), Estrogen receptor (ER), Progesterone receptor (PR), Endometrial histomorphology, Allred scoring, Hormonal imbalance, Proliferative endometrium.

INTRODUCTION

Abnormal uterine bleeding (AUB) is a prevalent gynecological issue affecting 10–30% of reproductive-aged women and nearly 50% of perimenopausal women . It includes variations in menstrual volume, frequency, and duration and is a frequent cause for endometrial sampling AUB may stem from structural or functional causes, which are now classified by FIGO's PALM-COEIN system Histopathology and immunohistochemistry play pivotal roles in evaluating endometrial abnormalities. Estrogen and progesterone regulate cyclical endometrial changes via their nuclear receptors, ER and PR, whose levels fluctuate across the menstrual cycle, ERα promotes proliferation, while PR counters estrogen effects, making receptor status clinically important Immunohistochemistry offers a practical method to assess receptor localization and intensity. DUB is often due to hormonal imbalance, which can be better elucidated through receptor profiling. Abnormal receptor expression is seen in hyperplasia and endometrial carcinoma. Assessing ER and PR in endometrial tissue not only aids diagnosis but also influences therapeutic planning PR positivity, in particular, is associated with better prognosis in endometrial carcinoma. This study aims to evaluate histomorphology and ER/PR receptor status in endometrial samples from AUB patients, offering insights into hormone-driven pathophysiology and potential for individualized therapy. This study aims to evaluate the histomorphology and ER/PR receptor status of the endometrium in AUB patients and correlate these findings. It also seeks to classify AUB causes and compare results with existing literature.

MATERIAL AND METHODS

This prospective observational study was conducted in the Department of Pathology, JLN Medical College and Hospital, Ajmer, Rajasthan, over a one-year period from January 2023 to December 2023. The study aimed to evaluate histopathological patterns of the endometrium and immunohistochemical expression of estrogen (ER) and progesterone (PR) receptors in women presenting with abnormal uterine bleeding (AUB). All women aged over 18 years presenting with AUB and from whom biopsy or hysterectomy specimens were received in the department during the study period were included. Patients with known bleeding or coagulation disorders, poorly fixed or autolyzed specimens, and those with incomplete clinical history or inadequate samples were excluded from the study. Ethical approval was obtained from the Institutional Ethical Committee before commencement.

Patient demographic details such as age, surgical procedure, and gross pathological features were recorded. All received specimens were fixed in 10% buffered formalin, processed routinely, and sectioned at 3–5 µm thickness using a semi-automated rotary microtome. These sections were stained with Hematoxylin and Eosin (H&E) for histopathological examination. Endometrial samples were histologically classified into proliferative, secretory, simple hyperplasia, complex hyperplasia, atypical hyperplasia, and endometrial carcinoma. Representative tissue blocks were selected for immunohistochemical (IHC) evaluation of estrogen and progesterone receptor expression.

The expression of ER and PR in the endometrial glandular and stromal cells was assessed using the Allred scoring system, which combines the proportion of positively stained nuclei with the intensity of staining. The proportion score ranged from 0 (none) to 5 (67–100% positive cells), and the intensity score ranged from 0 (no staining) to 3 (strong staining). The total Allred score was the sum of both scores, with scores of 0–2 considered negative and scores of 3–8 considered positive for receptor expression. This scoring allowed semi-quantitative evaluation of receptor distribution and intensity in various histological patterns of AUB. Statistical analysis was performed using PRIMER software. Qualitative variables such as histological patterns and receptor positivity were expressed as frequencies and percentages. Quantitative variables were reported as mean ± standard deviation (SD). Associations between receptor expression and histological patterns were evaluated using the chi-square test. A p-value <0.05 was considered statistically significant. This robust methodology enabled detailed assessment of the hormonal receptor profile in AUB and its correlation with histomorphological changes, thereby providing insight into potential therapeutic strategies.

RESULT

This prospective observational study was conducted from January to December 2023 at the Department of Pathology, JLN Medical College, Ajmer, Rajasthan, on 150 patients presenting with abnormal uterine bleeding (AUB). The study aimed to evaluate the histomorphological patterns of endometrium and correlate them with immuno-histochemical expression of estrogen and progesterone receptors (ER/PR).The majority of patients were between 41–50 years (52.67%) and had parity P3 (32.67%).

Menorrhagia was the most common bleeding pattern (59.33%), followed by postmenopausal bleeding (20.67%). Clinical diagnoses ranged from general AUB (47.33%) to AUB-L (16.67%) and DUB (15.33%). Functional causes of AUB were more common (71.33%) than organic (28.67%).

Table 1: Distribution of the Cases According to Causes and Histopathological Diagnosis of AUB

Causes	Number	Percentage %
Organic Causes	43	28.67
Functional Causes	107	71.33
Histopathological diagnosis		
Proliferative Endometrium	91	60.67
Disordered Proliferative Endometrium	22	14.67
Secretary Endometrium	22	14.67
Inconclusive	4	2.67
Endometrial Polyp	3	2
Atropic Endometrium	1	0.67
Complex Hyperplasia	1	0.67
Early Secretary Endometrium	1	0.67
Endometrial Adenocarcinoma	1	0.67
Endometrial Stromal Sarcoma	1	0.67
Late Secretary Endometrium	1	0.67
Simple Cystic Hyperplasia	1	0.67
Simple Hyperplasia	1	0.67
Total	150	100

Histopathologically, proliferative endometrium was predominant (60.67%), followed by secretory and disordered proliferative types (14.67% each). Malignant lesions were rare (endometrial adenocarcinoma and stromal sarcoma each 0.67%). No significant correlation was found between age, parity, or bleeding pattern and histological type.

Table 2: Association of Age With Histopathological Pattern

Histopathological Diagnosis	Total No.	18–40 years No. (%)	41–50 years No. (%)	> 50 years No. (%)	P Value	LS
Atrophic Endometrium	1	0 (0.00%)	1 (1.27%)	0 (0.00%)	0.644	NS
Endometrial Hyperplasia	3	1 (2.44%)	2 (2.53%)	0 (0.00%)	0.699	NS
Endometrial Adenocarcinoma	1	0 (0.00%)	1 (1.27%)	0 (0.00%)	0.644	NS
Endometrial Polyp	3	0 (0.00%)	1 (1.27%)	2 (7.14%)	0.092	NS
Endometrial Stromal Sarcoma	1	1 (2.44%)	0 (0.00%)	0 (0.00%)	0.269	NS
Inconclusive	4	0 (0.00%)	1 (1.27%)	1 (3.57%)	0.449	NS
Proliferative Endometrium	113	32 (78.05%)	57 (72.15%)	24 (85.71%)	0.333	NS
Secretory Endometrium	24	7 (17.07%)	16 (20.25%)	1 (3.57%)	0.119	NS
Total	150	41 (100%)	79 (100%)	28 (100%)		

Table 3: ER/PR Expression & Scoring Summary

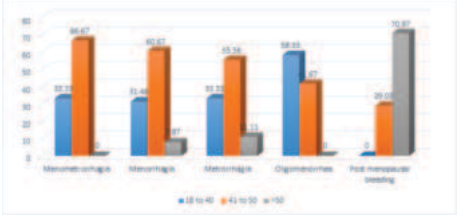
ER/PR Expression	Frequency	%
ER Positive	124	82.67
PR Positive	124	82.67
Dual Positive (ER+PR+)	119	79.33
Dual Negative (ER–PR–)	17	11.33
Tissue Washed Out (Invalid)	4	2.67
ER Allred Score 6 (Most Common)	51	34
PR Allred Score 6 (Most Common)	42	28
ER/PR in Malignant Lesions	Mostly Negative	2/3 cases neg
ER/PR in Proliferative Endometrium	ER+: 86.8%, PR+: 85.7%	High positivity

Immunohistochemical analysis revealed that 82.67% of cases were positive for both ER and PR. High Allred scores (6–8) were common, with ER score 6 in 34% and PR score 6 in 28%. Malignant cases showed negative ER/PR expression, indicating loss of hormonal dependency. Most benign cases showed strong receptor positivity, with 79.33% dual-positive. The study highlights the diagnostic value of ER/PR evaluation in AUB and potential for hormone-targeted therapy in receptor-positive cases

Table :4 Association of ER and PR Receptors with Histo-pathological Diagnosis

Histopathological Diagnosis	Total No	ER Positive No (%)	PR Positive No (%)
Atrophic Endometrium	1	0 (0.00%)	1 (100.00%)
Complex Hyperplasia	1	1 (100.00%)	1 (100.00%)
Disordered Proliferative Endometrium	22	17 (77.27%)	17 (77.27%)
Early Secretory Endometrium	1	1 (100.00%)	1 (100.00%)
Endometrial Adenocarcinoma	1	0 (0.00%)	0 (0.00%)
Endometrial Polyp	3	1 (33.33%)	2 (66.67%)
Endometrial Stromal Sarcoma	1	0 (0.00%)	0 (0.00%)
Inconclusive	1	0 (0.00%)	0 (0.00%)
Late Secretory Endometrium	1	1 (100.00%)	1 (100.00%)
Other	3	3 (100.00%)	3 (100.00%)
Proliferative Endometrium	91	79 (86.81%)	78 (85.71%)
Secretory Endometrium	22	20 (90.91%)	19 (86.36%)
Simple Cystic Hyperplasia	1	0 (0.00%)	0 (0.00%)
Simple Hyperplasia	1	1 (100.00%)	1 (100.00%)
Total	150	124 (82.67%)	124 (82.67%)

Overall, 82.7% of cases were positive for both ER and PR, indicating a high prevalence of hormone receptor expression in non-structural causes of AUB. Proliferative endometrium, the most common histological finding, showed ER positivity in 86.7% and PR positivity in 85.6% of cases. Similarly, secretory endometrium demonstrated strong positivity, with 90.9% for ER and 86.4% for PR.



Graph 1: Association of Age Group with Bleeding Pattern

Graph 2 : ER and PR Expression

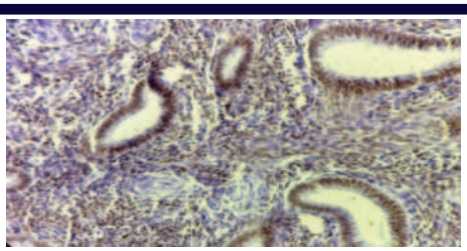


Fig 1: Immunohistochemical staining for Estrogen receptor (ER), demonstrating >80% of proliferative endometrium glands and stroma showing strong nuclear positivity.Alred Score-8/8 (40X)

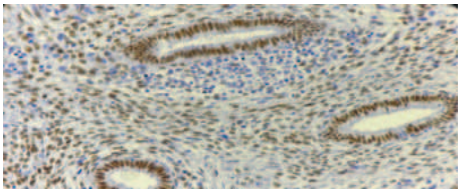


Fig 2: Immunohistochemical staining for Progestrogene receptor (PR), demonstrating >80% of proliferative endometrium glands and stroma showing strong nuclear positivity.Alred Score-8/8 (20X)

DISCUSSION

In the present study of 150 women with abnormal uterine bleeding (AUB), the majority of cases (52.67%) occurred in the 41–50 years age group, consistent with findings by Golecha and Porwal et al. (2018) who reported 56% cases in perimenopausal women Kumar et al. (2019) , and Gupta et al. (2024), who also observed a peak incidence in the 41–45 years bracket. This age-related prevalence likely reflects hormonal fluctuations and age-related uterine pathologies. Most patients were multiparous, with parity 2–4 accounting for 89% of cases, echoing trends noted by Shrestha et al. (2020), Singh et al. (2020) , and Sreedevi et al. (2024) , who also observed a predominance of AUB in multiparous women. Menorrhagia was the most common bleeding pattern (59.33%) in our cohort, in agreement with regional studies reporting heavy menstrual bleeding as a frequent presentation [69,70]. Histologically, the proliferative endometrium was the most common pattern (60%), comparable to findings by Dubey et al. (2018), Singh et al. (2020)[17], and Sreedevi et al. (2024)[18], indicating unopposed estrogen as a frequent underlying cause. No significant association was found between age or parity and histopathology ($P > 0.05$), consistent with earlier studies Shrestha et al.(2020), Singh et al.(2020) [16,17].

Estrogen receptor (ER) and progesterone receptor (PR) expression was observed in 83.33% of cases each, with ER+/PR+ co-expression noted in 80% of patients. This finding aligns with Shetty et al. (2018) , Mishra et al. (2022), and Singh et al. (2020) [17], who reported ER and PR positivity rates between 76%–85%. ER/PR expression was significantly reduced in malignant cases, where 9.52% showed receptor negativity. This supports prior evidence that loss of PR and ER is associated with malignancy or high-grade lesions Kumar et al. (2019), Chaudhary et al (2020) and Gupta et al.(2017)¨ . Overall, our findings reinforce the utility of integrating immunohistochemistry into the diagnostic workup of AUB to assess hormonal responsiveness, distinguish benign from malignant lesions, and guide hormone-based therapies.

SUMMARY AND CONCLUSION

In this prospective study most commonly affected age group was 41–50 years, and 89% of the patients had parity between P2 and P4. Menorrhagia was the most frequent bleeding pattern (59.33%), followed by postmenopausal bleeding (20.67%). Clinically, 47.33% of cases were classified as nonspecific AUB, while leiomyoma and dysfunctional uterine bleeding were also observed. Functional causes were predominant, accounting for 71.33% of cases. Histologically, proliferative endometrium was the most common pattern (60.67%), with no significant association between histology and either age or parity. Estrogen and progesterone receptor positivity was found in 83.33% of cases, with 80% showing dual ER+/PR+ expression. Malignant lesions were mostly ER/PR negative, indicating hormone-independent pathology. The study highlights the value of hormone receptor assessment in the diagnosis, prognosis, and management of AUB.

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