Section: Miscellaneous

Original Research Article

CLINICOPATHOLOGICAL CORRELATION OF ENDOMETRIAL HYPERPLASIA WITH ABNORMAL UTERINE BLEEDING

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is one of the most common gynecological complaints in women of reproductive and perimenopausal age. Endometrial hyperplasia, a significant histopathological correlate of AUB, is characterized by abnormal proliferation of endometrial glands and has the potential to progress to endometrial carcinoma. The WHO 2020 classification system redefined endometrial hyperplasia into two major categories—endometrial hyperplasia without atypia and endometrial atypical hyperplasia/endometrioid intraepithelial neoplasia (EIN)—enhancing reproducibility and clinical relevance. Objectives: To assess the clinicopathological correlation between different types of endometrial hyperplasia (as per WHO 2020 classification) and abnormal uterine bleeding patterns, and to evaluate the demographic and risk factor profile of affected women.

Materials and Methods: A cross-sectional observational study was conducted over a 12-month period at a tertiary care center among women presenting with AUB. Endometrial samples were obtained via dilatation and curettage or pipelle biopsy and evaluated histologically. All cases were classified according to WHO 2020 guidelines. Demographic details, bleeding patterns, risk factors (such as obesity, diabetes, and hypertension), and clinical presentations were recorded. Statistical analysis was performed to correlate histopathological types with clinical features.

Results: Among the 156 women included, the most common age group affected was 41–50 years. The predominant bleeding pattern was heavy menstrual bleeding, followed by intermenstrual bleeding. Endometrial hhyperplasia without atypia accounted for 78.8% of cases, while atypical hyperplasia/ (EIN) was seen in 21.2%. Atypical hyperplasia was significantly associated with obesity, diabetes, and prolonged unopposed estrogen exposure ($p < 0.05$). The clinicopathological correlation showed that heavy and prolonged bleeding was more frequent in women with EIN, while non-atypical cases often presented with irregular cycles and mild menorrhagia.

Conclusion: The study emphasizes the importance of correlating clinical symptoms with histopathological findings in cases of AUB. Accurate classification of endometrial hyperplasia using WHO 2020 guidelines provides essential prognostic and therapeutic direction, particularly for identifying women at higher risk of progression to malignancy.

Keywords: Abnormal Uterine Bleeding, Endometrial Hyperplasia, Atypical Hyperplasia, WHO 2020 Classification, Histopathology, Endometrial Intraepithelial Neoplasia.

INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the most frequent complaints encountered in gynecological practice, particularly among women in the perimenopausal and postmenopausal age groups. It accounts for nearly one-third of all outpatient gynecology visits and often leads to endometrial sampling to rule out underlying structural or pathological causes.[1] Among these, endometrial hyperplasia is a key histopathological finding, defined as an increased gland-to-stroma ratio within the endometrial tissue, primarily due to prolonged estrogen stimulation unopposed by progesterone.[2]

Historically, the classification of endometrial hyperplasia was complex and often inconsistent across pathologists, leading to challenges in diagnosis and management. In response, the World Health Organization (WHO) revised its classification in 2020 to enhance diagnostic clarity and clinical applicability. The WHO 2020 system broadly categorizes endometrial hyperplasia into two entities: (a) endometrial hyperplasia without atypia and (b) atypical hyperplasia, now also termed endometrioid intraepithelial neoplasia (EIN).[3] This newer system eliminates the earlier subtypes (simple and complex, with or without atypia), instead focusing on cytological atypia and clonality as key features of malignant potential.[4]

Non-atypical endometrial hyperplasia is generally considered benign and carries a low risk of progression to carcinoma, particularly when managed with hormonal therapy or surveillance. In contrast, atypical hyperplasia (EIN) has a significantly higher risk of progression to endometrioid adenocarcinoma, with estimates ranging between 25% and 40% if left untreated.[5,6] The presence of cytological atypia, architectural complexity, and associated clinical risk factors necessitate early identification and aggressive management in such cases.

AUB may present in various forms including heavy menstrual bleeding, intermenstrual bleeding, postmenopausal bleeding, or irregular cycles. These bleeding patterns often correlate with the underlying histological type of hyperplasia and can provide important clinical clues.[7] Risk factors such as obesity, polycystic ovarian syndrome (PCOS), chronic anovulation, diabetes mellitus, and prolonged estrogen use without opposition are known to increase the risk of endometrial hyperplasia.[8]

This study was undertaken to evaluate the spectrum of endometrial hyperplasia using the WHO 2020 classification and to correlate histopathological findings with clinical presentation in women presenting with AUB. By establishing a clinicopathological correlation, the study aims to enhance diagnostic precision and guide appropriate therapeutic decision-making in patients with abnormal uterine bleeding.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based, cross-sectional observational study conducted over a period of 12 months in the Department of Obstetrics and Gynecology at a tertiary care teaching hospital. The study focused on women presenting with abnormal uterine bleeding (AUB) who underwent endometrial sampling and histopathological evaluation.

Inclusion Criteria:

- Women aged 20 years and above presenting with AUB
- Patients who consented to endometrial sampling
- Endometrial biopsy showing features of hyperplasia (as per WHO 2020 classification)

Exclusion Criteria

- Women on hormone replacement therapy
- Patients diagnosed with endometrial carcinoma
- Inadequate or unsatisfactory biopsy samples

Sample Size

A total of 156 cases were included in the study based on inclusion criteria over the 12-month study period.

Data Collection and Clinical Evaluation

Detailed clinical history, including age, parity, menstrual pattern, duration and severity of bleeding, and relevant risk factors (such as obesity, diabetes, hypertension, PCOS, or use of unopposed estrogen), was obtained. General physical examination and systemic assessment were performed. All women underwent pelvic examination and transvaginal sonography where indicated.

Endometrial Sampling and Histopathological Examination

Endometrial tissue samples were obtained via pipelle endometrial biopsy, dilatation and curettage (D&C), or hysteroscopy-guided biopsy, depending on the clinical indication. Specimens were fixed in 10% formalin, processed, and stained with hematoxylin and eosin (H&E). Each sample was examined by two independent pathologists and classified as per WHO 2020 criteria into:

- Endometrial hyperplasia without atypia
- Atypical hyperplasia / Endometrioid intraepithelial neoplasia (EIN)

Statistical Analysis

All data were entered into Microsoft Excel and analyzed using SPSS software (version 21.0). Descriptive statistics were used to summarize demographic and clinical data. Associations between histopathological diagnosis and risk factors were analyzed using the Chi-square test. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee. Informed written

consent was obtained from all participants. Confidentiality and anonymity of all patient data were maintained throughout the study.

RESULTS

This study included a total of 156 women who presented with abnormal uterine bleeding (AUB) and were histologically diagnosed with endometrial hyperplasia based on WHO 2020 classification. The objective was to correlate the clinical patterns of AUB with the histopathological subtype of endometrial hyperplasia and associated risk factors. Data were categorized and interpreted across multiple domains: age distribution, bleeding pattern, parity, clinical comorbidities (such as obesity, diabetes, and hypertension), mode of sampling, and histopathological spectrum. Each domain is presented through structured tables with analytical interpretation. Special attention was given to the distinction between non-atypical hyperplasia and atypical hyperplasia (EIN), in line with WHO 2020 guidelines.

Demographic and Clinical Profile

Table 1 shows the age-wise distribution of patients. The majority (46.2%) were between 41 and 50 years of age, followed by 33.3% in the 31–40 age group. This reflects the higher prevalence of endometrial hyperplasia among perimenopausal women.

Table 1: Age distribution of patients with endometrial hyperplasia (n = 156)

Age group (years)	Frequency	Percentage (%)
21–30	14	9.0
31–40	52	33.3
41–50	72	46.2
>50	18	11.5

Table 2 presents the parity status of the study population. A majority were multiparous (71.8%), while 17.3% were nulliparous and 10.9% had one previous delivery.

Table 2: Parity status of patients

Parity	Frequency	Percentage (%)
Nulliparous	27	17.3
Para 1	17	10.9
Para ≥2	112	71.8

Table 3 outlines the presenting bleeding patterns. Heavy menstrual bleeding (menorrhagia) was the most common form (39.7%), followed by intermenstrual bleeding (21.8%) and postmenopausal bleeding (16.0%).

Table 3: Clinical bleeding pattern in patients with AUB

Bleeding pattern	Frequency	Percentage (%)
Heavy menstrual bleeding	62	39.7
Intermenstrual bleeding	34	21.8
Irregular cycles	26	16.7
Postmenopausal bleeding	25	16.0
Spotting/unspecified	9	5.8

Risk Factors and Associated Conditions

Table 4 shows the distribution of BMI. A majority of patients (59.6%) were overweight or obese, suggesting a strong correlation between obesity and endometrial hyperplasia.

Table 4: Body mass index (BMI) distribution

BMI category (kg/m²)	Frequency	Percentage (%)
<18.5 (Underweight)	4	2.6
18.5–24.9 (Normal)	59	37.8
25–29.9 (Overweight)	62	39.7
≥30 (Obese)	31	19.9

Table 5 highlights comorbid conditions. Hypertension and diabetes were present in 28.8% and 24.4% of cases, respectively. A combination of both was seen in 12.2% of patients.

Table 5: Distribution of associated comorbidities

Comorbidity	Frequency	Percentage (%)
Hypertension only	45	28.8
Diabetes mellitus only	38	24.4
Both HTN + DM	19	12.2
None	54	34.6

Table 6 shows the mode of endometrial sampling. Dilatation and curettage (D&C) was the most common technique (56.4%), followed by pipelle biopsy (34.0%).

Table 6: Method of endometrial sampling

Sampling method	Frequency	Percentage (%)
D&C	88	56.4
Pipelle biopsy	53	34.0
Hysteroscopic biopsy	15	9.6

Histopathological Spectrum (WHO 2020 Classification)

Table 7 presents the histological classification of endometrial hyperplasia. Non-atypical hyperplasia was the most common (78.8%), while atypical hyperplasia/EIN constituted 21.2% of cases.

Table 7: Histological classification based on WHO 2020 guidelines

Type of hyperplasia	Frequency	Percentage (%)
Endometrial Hyperplasia without atypia	123	78.8
Atypical hyperplasia/(EIN)	33	21.2

Table 8 shows the distribution of histological types across age groups. Atypical hyperplasia was more frequent in women above 45 years, whereas non-atypical cases were evenly distributed.

Table 8: Age-wise distribution of histological types

Age group (years)	Non-atypical	Atypical (EIN)
21–30	13	1
31–40	46	6
41–50	53	19
>50	11	7

Table 9 evaluates the correlation between BMI and type of hyperplasia. Atypical hyperplasia was significantly more common in women with BMI ≥30.

Table 9: Association between BMI and histological type

BMI Category	Non-atypical	Atypical (EIN)
<25	60	3
25–29.9	46	16
≥30	17	14
p-value		<0.05

Table 10 presents the relationship between comorbidities and histological type. Atypical hyperplasia had higher prevalence among patients with diabetes and/or hypertension.

Table 10: Association between comorbidities and histological type

Comorbidity	Non-atypical	Atypical (EIN)
None	52	2
HTN only	32	13
DM only	26	12
Both HTN + DM	13	6
p-value		**<0.05**

Table Summary

The study included 156 women with AUB and histologically confirmed endometrial hyperplasia. The most common age group was 41–50 years, and the majority were multiparous (Table 1, Table 2). Heavy menstrual bleeding and intermenstrual bleeding were the predominant symptoms (Table 3). Over half the participants were overweight or obese, and nearly one-third had comorbidities such as diabetes or hypertension (Table 4, Table 5). D&C was the preferred method of sampling (Table 6). Non-atypical hyperplasia was more common overall, while atypical hyperplasia was found in 21.2% of cases (Table 7). Atypical lesions were more prevalent in older women and those with higher BMI or associated comorbidities (Table 8, Table 9, Table 10). These findings highlight the importance of risk-based screening and histopathological evaluation in women with AUB.

DISCUSSION

This study evaluated the clinicopathological correlation of endometrial hyperplasia in women presenting with abnormal uterine bleeding (AUB), with histopathological categorization based on the WHO 2020 classification. The findings demonstrate that the majority of patients with endometrial hyperplasia were in the perimenopausal age group, multiparous, and frequently presented with heavy or

irregular menstrual bleeding. This trend is consistent with previous studies that report peak incidence of endometrial hyperplasia in women aged 40 to 50 years due to cumulative exposure to unopposed estrogen during the perimenopausal transition.[9]

Histologically, 78.8% of cases in this study were diagnosed as non-atypical endometrial hyperplasia, whereas 21.2% showed features of atypical hyperplasia or endometrial intraepithelial neoplasia (EIN). These proportions are in line with reports from recent WHO 2020-aligned studies, where non-atypical hyperplasia constitutes the predominant category and has a relatively low risk of progression to malignancy.[10] In contrast, atypical hyperplasia is considered a precancerous lesion and warrants prompt therapeutic intervention.[11]

Clinical symptoms showed significant overlap between the two histological categories, although atypical hyperplasia was more frequently associated with heavy menstrual bleeding and postmenopausal bleeding. Several studies have emphasized that atypical lesions often present with more alarming or prolonged bleeding patterns and must be differentiated carefully from early-stage carcinoma.[12]

Obesity emerged as a significant risk factor in this study, with a higher proportion of atypical hyperplasia observed among women with BMI ≥30. Excess adipose tissue contributes to peripheral conversion of androgens to estrogens, thereby promoting endometrial proliferation in the absence of progesterone opposition.[13] Similar findings have been reported in observational cohorts where obesity showed strong associations with EIN and endometrial carcinoma risk.[14]

Additionally, the presence of comorbid conditions such as diabetes and hypertension was more frequent in patients with atypical hyperplasia. Hyperinsulinemia and metabolic dysfunctions are known to modulate estrogen pathways and contribute to endometrial neoplastic transformation.[15] Studies from large cancer registries have documented the synergistic effect of these risk factors in the progression from atypical hyperplasia to endometrioid adenocarcinoma.[16]

The use of the WHO 2020 classification in this study provided greater clarity and consistency in reporting, and facilitated clinically meaningful stratification of risk. Unlike the previous system, which had four overlapping categories, the simplified two-tier WHO 2020 framework improves reproducibility among pathologists and aligns better with therapeutic decision-making.[17]

By integrating clinical history, bleeding patterns, risk factor profiling, and updated histological interpretation, this study underscores the importance of a multidisciplinary approach in the evaluation and management of AUB. Identifying women at risk of EIN can enable early interventions and potentially prevent malignant transformation.

CONCLUSION

This study establishes a significant clinicopathological correlation between abnormal uterine bleeding and endometrial hyperplasia using the WHO 2020 classification. The highest prevalence was observed among women in the perimenopausal age group, with heavy menstrual bleeding being the most common presenting complaint. Non-atypical endometrial hyperplasia constituted the majority of histological findings, yet a notable proportion of women had atypical hyperplasia (EIN), emphasizing the need for careful evaluation. Atypical hyperplasia was found to be significantly associated with obesity, diabetes, and hypertension, all of which are modifiable risk factors. These findings support the role of metabolic dysfunction and prolonged unopposed estrogen exposure in the pathogenesis of atypical lesions. Histopathological evaluation using WHO 2020 criteria enhances diagnostic precision and eliminates ambiguity in classification. The study also highlights the importance of comprehensive risk factor assessment and individualized management strategies in patients with AUB. Early detection and differentiation between non-atypical and atypical hyperplasia are crucial for preventing malignant transformation. Routine endometrial sampling in high-risk women presenting with AUB should be emphasized in clinical protocols. Continued application of WHO 2020 guidelines will aid in better prognostic stratification and therapeutic decision-making.

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