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ARTICLE

Histopathological Patterns of Endometrial Samples among Women with Abnormal Uterine Bleeding

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ABSTRACT

Background: For women who have abnormal uterine bleeding (AUB) the first step to determine whether uterine changes are functional or benign is to perform a tissue diagnosis by looking at the endometrium.
Objective: To outline the range of endometrial pathologies obtained in women with AUB and analyze the distribution of these pathologies by age group.
Methods: This is the retrospective cross-sectional study that involved 300 endometrial samples collected from women who had AUB at Mosul General Hospital, Mosul, Iraq, during 18 months (from January 2025 to June 2026). Specimens were routinely processed and stained with hematoxylin and eosin and reviewed independently by two pathologists. Six ages groups were used to tabulate diagnoses. The chi-square test or Fisher's exact test was used to test for associations between age and diagnostic category; a P value of < 0.05 was accepted as significant.
Results: AUB was most frequent at 40–49 years (46.7%), followed by 50–59 years (22.0%). The most frequently reported were hormonal imbalance (112 cases, 37.3%), endometrial polyp (44, 14.7%), proliferative-phase endometrium (39, 13.0%) and secretory-phase endometrium (26, 8.7%). There were 17 cases (5.7%) with hyperplasia without atypia, five (1.7%) with atypical hyperplasia/endometrial intraepithelial neoplasia (EIN), and 12 (4.0%) with endometrial carcinoma, for a total of 34 (11.3%) cases of premalignant and malignant lesions. 83.3% of the 10 cases of carcinoma in women were at the old age group of 50 years and above. Women aged ≥50 years had a higher prevalence of premalignant or malignant lesions compared with women aged <50 years (24.7% vs 6.0%), with the overall distribution of diagnostic categories being significantly different between the two age groups ($P < 0.001$).
Conclusion: Functional and benign changes were more common than hyperplasia or carcinoma (approximately 1 in 9 specimens had these changes) and an increased risk was seen with age. Histologic evaluation of endometrial tissue continues to be the mainstay of the work-up of AUB, especially for women older than 50 years.

Introduction

Abnormal uterine bleeding (AUB) is a disruption of the usual pattern of menstruation in women who are not pregnant, in terms of regularity, duration, frequency or amount. It is one of the most common complaints that women seek medical advice about and can have a significant impact on women's physical health and quality of life. To provide some uniformity in evaluation of its causes, the International Federation of Gynecology and Obstetrics (FIGO) has developed the PALM-COEIN system. Structural causes (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia) and non-structural causes (coagulopathy, ovulatory dysfunction, primary endometrial disorders, iatrogenic causes and causes not otherwise classified) are

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separated (1, 2). The endometrium is very responsive to ovarian steroid hormones, and is affected by age, hormonal status and sampling time. In women with abnormal uterine bleeding, it often demonstrates normal proliferative or secretory changes, but also may demonstrate functional hormonal disturbance, chronic inflammation, polyps, atrophy, hyperplasia, and carcinoma. Correct distinction is clinically important as treatment can vary from reassurance and medical treatment to hysteroscopic surgery, long term monitoring or definitive oncological treatment. A diagnosis of premalignant and malignant lesions is confirmed by microscopic examination of tissue. The current WHO classification distinguishes between endometrial hyperplasia without atypia and atypical hyperplasia/endometrial intraepithelial neoplasia (EIN) and is based primarily on the risk of progression to endometrial carcinoma (3). There is variation in the published frequencies of the different histological patterns, which is partly due to the differences in age, referral patterns, sampling methods and diagnostic terminology among the various studies (4–11). The diagnosis of the series in Iraq has been mostly functional and benign, while a small percentage of patients found pre-malignancy or malignancy (4, 5). Recent age-stratified data from the Mosul area, however, are scarce and local data are required as the population characteristics and metabolic risk factors in patients from northern Iraq may be different from those reported elsewhere. For this reason, 300 endometrial samples were collected from women with AUB, who were attending Mosul General Hospital.

General objective: To outline the range of endometrial histology seen in women presenting with AUB and appreciate the age distribution.

Specific objectives: (1) To identify the incidence of benign, functional, premalignant and malignant endometrial diagnoses in the study population. (2) To assess the relationship between age group and endometrial lesion (non-neoplastic, hyperplasia without atypia, atypical hyperplasia/EIN, and carcinoma). (3) To find out the age distribution and frequency of endometrial hyperplastic (with and without atypia) and endometrial carcinoma in this institution.

Methods

Study design and setting

It was a cross sectional retrospective study of archived records conducted in the Pathology Department at Mosul General Hospital, Mosul, Iraq. The study was conducted over 18 months January 2025 - June 2026.

Study population and sample

All 300 endometrial specimens obtained by dilatation and curettage (D&C) from women with a clinical diagnosis of AUB during the study period were assessed, and each woman was assessed as having one final histological diagnosis. The sample size of 300 was selected because all consecutive eligible specimens were received during the 18 months, expected prevalence, and margin of error used were specified.

Inclusion criteria: (1) a clinical diagnosis of AUB (abnormality of the regularity, frequency, duration or volume of bleeding); (2) the presence of an endometrial specimen that was interpretable following D&C; and (3) the age at the time of sampling was recorded.

Exclusion criteria: (1) Clinical and histological evidence of pregnancy (retained products of conception, ectopic pregnancy and gestational trophoblastic disease); and (2) specimens that were too small, crushed and/or autolyzed to make a definite diagnosis.

Tissue processing and histopathological analysis

Endometrial tissue collected with D&C was immediately fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin, cut 4 μm and stained with hematoxylin and eosin (H&E). The slides were independently examined by two experienced pathologists, and a consensus diagnosis was made for each case. Eleven categories of diagnosis were made:

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atrophic endometrium, atypical hyperplasia/EIN, chronic endometritis, hormonal imbalance (functional pattern), endometrial carcinoma, endometrial hyperplasia without atypia, endometrial polyp, menstrual-type endometrium (breakdown), proliferative-phase endometrium, and secretory-phase endometrium. The hyperplasia was categorized as the standard classification proposed by WHO (3).

Data collection

Data on age and final histopathology diagnosis were obtained from the department's archives on a structured data collection sheet. Women were assigned to six predefined age groups: <30, 30–39, 40–49, 50–59, 60–69, and ≥70 years. In order to compare women, they were also dichotomized at 50 years of age (less than 50 vs 50 years or more), as a proxy for the menopausal transition, since menopausal status was not available in the archived files. Additionally, diagnoses were classified for analysis into four categories: non-neoplastic/other benign lesions, hyperplasia without atypia, atypical hyperplasia/EIN, and endometrial carcinoma.

Statistical analysis

Data was analyzed on MS Excel. Categorical variables are displayed in absolute (n) frequencies and relative percentages (%). The association between age group and diagnostic category was explored using Pearson's chi-square test in the table had expected counts less than 5. The odds ratio (OR) and 95% confidence interval (CI) were determined for premalignant/malignant lesions and for carcinoma in women aged ≥50 years compared to <50 years. Statistically significant P value was defined as <0.05. (IBM SPSS version 32).

Ethical considerations

Ninewa Health Directorate/Mosul General Hospital Ethics and Research Committee approved the study protocol (Number: 58545, Date: 8/12/2024).

Results

Age distribution

Women with AUB had a total of 300 endometrial specimens tested. The women ranged in age from the reproductive years to postmenopause, with the largest age group being the fifth decade. Women aged 40–49 years formed the largest subgroup (n = 140, 46.7%), followed by those aged 50–59 years (n = 66, 22.0%) and 30–39 years (n = 48, 16.0%). Women younger than 30 years accounted for 9.0% (n = 27) and women aged 60 years or older for 6.3% (n = 19) (Table 1).

Table 1. Distribution of the study sample by age group (n = 300)

Age group (years)	Number	Percentage
<30	27	9.0
30–39	48	16.0
40–49	140	46.7
50–59	66	22.0
60–69	17	5.7
≥70	2	0.7
Total	300	100.0

Histopathological spectrum

The range of diagnosis is presented in Table 2. The commonest disorders were non-neoplastic functional disorders and benign conditions. The most common diagnosis was

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hormonal imbalance (112 cases, 37.3%) followed by endometrial polyp (44 cases, 14.7%). There were 65 case of normal cyclic endometrium, which included 39 (13.0%) of proliferative phase and 26 (8.7%) of secretory phase endometrium. 23 cases (7.7%) had disordered proliferative endometrium.

Table 2. Histopathological spectrum of the examined endometrial specimens (n = 300)

Histopathological diagnosis	No. of cases	Percentage
Hormonal imbalance	112	37.3
Endometrial polyp	44	14.7
Proliferative-phase endometrium	39	13.0
Secretary-phase endometrium	26	8.7
Disordered proliferative endometrium	23	7.7
Endometrial hyperplasia without atypia	17	5.7
Endometrial carcinoma	12	4.0
Atrophic endometrium	10	3.3
Chronic endometritis	9	3.0
Atypical hyperplasia/EIN	5	1.7
Menstrual-type endometrium (breakdown)	3	1.0
Total	300	100.0

Premalignant and malignant lesions and age

The majority of the pre-malignant and malignant lesions were seen in the older groups of age. Endometrial hyperplasia without atypia was seen in 17 cases (5.7%), 16 cases (94.1%) of which were in women aged 40–59 years. Five cases (1.7%) had an atypical hyperplasia/EIN diagnosis, and 4 of them (80.0%) were women of 50 years or older. Endometrial carcinoma was diagnosed in 12 cases (4.0%); 10 of the 12 (83.3%) were diagnosed in women aged 50 years or older, most of whom were in the age group of 60-69 years (6 cases). In total, 300 specimens, 11.3% (34 of 300) demonstrated hyperplasia or carcinoma (17 patients with hyperplasia that was not atypical, 5 patients with atypical hyperplasia/EIN, and 12 patients with carcinoma) and 61.8% (21 of 34) of these were in women of age ≥50 years. There was a significant difference between the distribution of the diagnostic categories of women under 50 years and those 50 years or older ($\chi^2 = 28.2$, df = 3, $P < 0.001$; Table 3). Premalignant or malignant lesions (hyperplasia, atypical hyperplasia/EIN, or carcinoma) were found in 13 of 215 women aged <50 years (6.0%) and in 21 of 85 women aged ≥50 years (24.7%) (OR 5.10, 95% CI 2.42–10.76; $\chi^2 = 21.1$, $P < 0.001$). Carcinoma alone was found in 2 of 215 women aged <50 years (0.9%) and in 10 of 85 women aged ≥50 years (11.8%) (OR 14.2, 95% CI 3.04–66.3; Fisher's exact test $P < 0.001$). There was no significant difference in the numbers of cases with hyperplasia without atypia in the two age groups (4.7% vs 8.2%, $P = 0.27$). When the six age groups were compared, the association between age group and diagnostic category was also significant ($\chi^2 = 97.7$, df = 15; Monte Carlo exact $P < 0.001$).

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Table 3. Diagnostic category by age group (<50 vs ≥50 years)

Diagnostic category	<50 years n (%)	≥50 years n (%)	P value
Non-neoplastic / other benign	202 (94.0)	64 (75.3)	
Hyperplasia without atypia	10 (4.7)	7 (8.2)	
Atypical hyperplasia/EIN	1 (0.5)	4 (4.7)	
Endometrial carcinoma	2 (0.9)	10 (11.8)	
Total	215 (100)	85 (100)	<0.001*

*Pearson chi-square test across the four categories ($\chi^2 = 28.2$, df = 3); the Monte Carlo exact P value was also <0.001.EIN, endometrial intraepithelial neoplasia.

Diagnostic patterns by age group

The histological diagnosis of each age group is shown in Table 4 and the increase in premalignant and malignant lesions with age is illustrated in Figure 1. Hormonal imbalance was the most common diagnosis at 40–49 years (61/140, 43.6%), followed by endometrial polyp (20/140, 14.3%). At 50–59 years hormonal imbalance (20/66, 30.3%) and polyp (16/66, 24.2%) remained the leading diagnoses. In women 60–69 years of age, the pattern became different: there were 6 of 17 samples of women with carcinoma, and 3 of 17 women with atrophic endometrium and atypical hyperplasia/EIN respectively. For reasons of completeness, the two women aged ≥70 years are described.

Table 4. Distribution of histological patterns by age group (n = 300)

Pattern	<30	30–39	40–49	50–59	60–69	≥70	Total
Atrophic endometrium	0	0	1	6	3	0	10
Atypical hyperplasia/EIN	0	0	1	1	3	0	5
Chronic endometritis	2	1	6	0	0	0	9
Disordered proliferative	0	3	13	7	0	0	23
Endometrial carcinoma	0	1	1	3	6	1	12
Hyperplasia without atypia	0	0	10	6	1	0	17
Endometrial polyp	1	4	20	16	2	1	44
Hormonal imbalance	8	23	61	20	0	0	112
Menstrual-type endometrium	0	0	3	0	0	0	3
Proliferative phase	12	6	14	6	1	0	39
Secretory phase	4	10	10	1	1	0	26
Total	27	48	140	66	17	2	300

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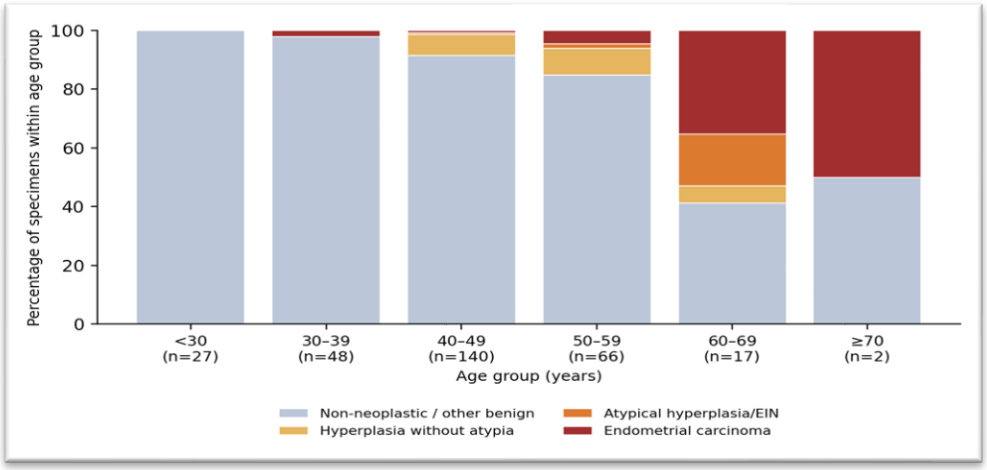


Figure 1. Percentage of specimens in each diagnostic category by age group. The proportion of hyperplasia and carcinoma increases from the fifth decade onward. The ≥70 group (n = 2) is shown for completeness only.

Discussion

Functional and benign endometrium were found to be the majority in this series of 300 endometrial specimens obtained from women with AUB in Mosul, while hyperplasia or carcinoma was present in 11.3% of patients, and was significantly more common in women over 50 years of age. These results are consistent with regional and international reports, and the points of agreement and difference are discussed below.

Age distribution: The peak occurred at 40–49 years (46.7%). In Pakistan, Riaz et al reported that majority of AUB women were in 40-50 years age group (7) and in Saudi Arabia, biopsy samples were classified by age by Husain et al and stressed the importance of biopsy sampling in women >40 years (6). It is a peak time when there is a decrease in the number of follicles and the body has intermittent anovulation with unopposed estrogen exposure, which is during the perimenopausal transition. This mechanism is a possible explanation for the prevalence of functional hormonal imbalance (37.3%) and disordered proliferative endometrium (7.7%) in this population.

Functional and benign patterns: Similar series of 288 women in Baghdad also showed the most common non-organic diagnosis as functional patterns, with proliferative endometrium (24.7%) and secretory endometrium (9.4%) found most frequently (4). There were some differences between that series and ours with respect to the organic diagnosis, as pregnancy-related specimens were included, making this a large proportion of their organic diagnosis, while pregnancy-related specimens were not included in our series. The study in Hillah showed that the correlation between the bleeding pattern and histological result was different for various age groups (5). On the other hand, Riaz et al. reported chronic endometritis as the most common diagnosis (35.2%) (7) which was only 3.0% in our series. The researchers noted that the discovery was due to regional socioeconomic and hygienic factors. Additionally, while we did not test it in our setting, differences in case mix and in the definition of chronic endometritis (using plasma cell immunostaining included) may be responsible. The second most commonly reported diagnosis was polyps with 14.7% of the cases found, and most commonly, between the ages of 40 and 59. This is higher than the 5.9% reported from Baghdad (4).

Endometrial polyps: are the "P" in PALM-COEIN and known as a structural cause of AUB (1-2). Blind curettage can either cause the polyps to fragment or overlook focal lesions, while hysteroscopy may be preferable if a focal lesion is suspected (13). The incidence of polyps may therefore vary from center to center depending on the method of sampling used.

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Normal cyclic endometrium: Combined, the proliferation and secretory phases of the endometrium comprised 21.7% of the specimens. This suggests that there is an important group of women with AUB who do not have an underlying endometrial abnormality. Their bleeding might be due to endocrine changes that are transient, structural disease outside the endometrium (like leiomyoma or adenomyosis) or sampling. It emphasizes the importance of considering the histology in conjunction with the menstrual history, pelvic ultrasound and clinical examination.

Hyperplasia and atypia: Hyperplasia without atypia (5.7%) was about three times as frequent as atypical hyperplasia/EIN (1.7%). The proportions for the Baghdad series of 5.6% non-atypical and 1.4% atypical hyperplasia (4) are similar. In addition, Riaz et al. determined that the majority was non-atypical hyperplasia (24.3% of their cases; 76 of 78). It is clinically important to separate the two entities. Women with atypical hyperplasia have significantly increased current and future risk of endometrial cancer compared with women with hyperplasia without atypia (12) and the WHO classification reflects this difference (3). Hyperplasia without atypia is typically treated medically and monitored; hyperplasia with atypia/EIN should be treated surgically and/or monitored closely. In the reports of a pathologist, consistent terms are important.

Carcinoma and age: The 4.0% of specimens that were analyzed were diagnosed as Endometrial carcinoma, with 10/12 (83.3%) of those specimens found in women 50 years or older. The odds of carcinoma were 14 times higher in women aged ≥50 years compared to younger women (OR 14.2, 95% CI 3.04–66.3); the large CI range was due to the low number of events. The incidence was higher than that of Baghdad (one carcinoma in 288 specimens, 0.3%) (4) but lower than in the Kosovo series of Latifi et al., in which 12 of 79 women (15.2%) had malignancy (8) and lower than in the Pakistani series in which 39 cancers were found in 321 specimens (about 12%) (7). Interestingly, Latifi et al. identified 10 of 12 malignancies (83.3%) in postmenopausal women (8), a rate that was similar to our 10 of 12 malignancies (83.3%) in women aged ≥50 years. Variations in absolute frequencies between series are likely due to differences in referral patterns, the age distribution of the women sampled, and to the exclusion of pregnancy-related specimens, as occurred in our study (4, 7, 8). Our results are also consistent with previous studies such as a Jordanian series, which also showed that the benign and malignant bleeding is more common in younger and older women, respectively, (9, 10). These data corroborate the need for expedient endometrial sampling in AUB women, 50 years or older. Group aged ≥70 years. In this group, only two women were part of this group, so the percentage are descriptive and should not be interpreted as population estimates.

Clinical implications

Pathologists will find the findings reassuring, as they give justification to the existing WHO terminology for hyperplasia, and to full reporting of atypia. If carcinoma is found, it is important to report the histological type and grade as this dictates the treatment pathway (14). In the woman who has persistent AUB, a benign or functional biopsy should not rule out a focal structural lesion and should be interpreted with this in mind; however, pelvic ultrasound or hysteroscopy should be considered.

Strengths and limitations

Advantages are the use of consensus diagnoses, the application of WHO terminology for hyperplasia, and the age-stratified analysis and formal statistical testing. There are several restrictions to be noted. First, the study was retrospective and single center, and the archived records were lacking in body mass index, parity, comorbidities including diabetes and hypertension, exogenous hormone use, bleeding pattern and ultrasound endometrial thickness measurements, which prevented the examination of risk factors. Second, it was not reported whether women were menopausal, and age 50 was used as a proxy. Thirdly, there were specimens collected via blind D&C which is less sensitive than hysteroscopy guided biopsy in identifying focal lesions. Fourth, the numbers in some cells

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(especially atypical hyperplasia/EIN) were small, resulting in large confidence intervals. Lastly, the sample may not be representative of all women with AUB in the community as they were sampled at a referral hospital.

Future directions

Further multicenter prospective studies with clinical risk factors and ultrasound measured endometrial thickness and with hysteroscopic correlation are required. The follow-up of women with atypical hyperplasia would also help to define local treatment response in northern Iraq.

Conclusion

The most common endometrial patterns in AUB patients were non-neoplastic and functional patterns, which were represented by hormonal imbalance and endometrial polyps, respectively, in Mosul. In 11.3% of cases, however, hyperplasia was detected, and there was a significantly greater risk of carcinoma in women more than 50 years old, with a particularly high risk in this group. Therefore, the histological evaluation of the endometrial biopsy is a valuable requisite for the exclusion of neoplasia and for the management in women with AUB.

Recommendations

Histology from the endometrium must be evaluated in the context of the patient's clinical symptoms. Should be evaluated in conjunction with the woman's age, menopausal status, bleeding history, and transvaginal ultrasound, and should be considered when the endometrium is thin in sampling women aged 50 years and older.

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Credit authorship contribution statement

Shafaq contributed to the study conception and design. Omnia collected the data. Ban performed the statistical analysis. Abeer interpreted the results and drafted the manuscript. All authors critically revised the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

Data availability

The data used in this study were collected from the archived data of Mosul General Hospital, Mosul, Iraq. The data were not publicly available as patient confidentiality and institutional regulations prevented it, but can be requested from the corresponding author with permission from the institution.

Declaration of AI usage

The authors employed AI to enhance the grammar, sentence flow and readability of Abstract and Discussion sections. The authors have read and edited all suggestions made.

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