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To Study the Histomorphological Spectrum and Role of BCl2 and Ki67 in Cases of Abnormal Uterine Bleeding at a Tertiary Care Centre

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Abstract: ***Introduction**: Abnormal uterine bleeding (AUB) encompasses irregularities in menstrual frequency, duration, and volume, and is a common gynecological complaint, especially in perimenopausal women. The histopathological examination of endometrial biopsies plays a pivotal role in determining the underlying cause, whether functional or organic. **Aims and Objectives**: 1) To evaluate the clinical and histomorphological spectrum in cases of abnormal uterine bleeding. 2) To study the role of BCl 2 and Ki 67 in cases of abnormal uterine bleeding. **Methodology**: A prospective cross-sectional study was conducted in the Department of Pathology, LLRM Medical College, Meerut in collaboration with the Department of Obstetrics and Gynaecology, SVBP Hospital Meerut. A total of 150 endometrial biopsy samples from women aged above 18 years with AUB were analyzed over a period of one year. Patients with AUB due to gestational causes or inadequate samples were excluded. Histopathological and immunohistochemical analysis was performed. **Results**: Among the 150 patients, 76 cases (50.7%) were of perimenopausal age group, 60 cases (40%) of reproductive-age group, and 14 cases (9.3%) of postmenopausal age group. Menorrhagia was the most common bleeding pattern (67.3%), followed by metrorrhagia (17.3%). Functional causes were predominant (64%), including proliferative endometrium (24.7%) and disordered proliferative endometrium (20%). Organic causes constituted 36%, with endometrial polyps (16.7%) and endometrial hyperplasia (8.6%) being most frequent. Endometrial carcinoma was seen in 4% of cases. BCl 2 expression was most commonly observed in functional causes, where 43.8% of cases were positive while Ki 67 expression commonly seen in organic causes where 46.3% of cases were positive. **Conclusion**: AUB was most prevalent in the perimenopausal age group and was predominantly due to functional endometrial causes. Histopathological evaluation remains essential for accurate diagnosis and appropriate treatment, particularly to rule out hyperplasia and malignancy. **Recommendations**: Routine endometrial sampling and histopathological examination should be performed in all women with AUB, particularly in perimenopausal and postmenopausal groups. Immunohistochemistry should be considered in cases with atypia or suspicion of malignancy to enable timely diagnosis and intervention.*

Keywords: Abnormal uterine bleeding, perimenopausal women, endometrial carcinoma

1. Introduction

Abnormal uterine bleeding (AUB) is a broad term that describes irregularities in the menstrual cycle involving the parameters of frequency, regularity, duration and volume of flow outside of pregnancy in reproductive-aged women. Abnormal uterine bleeding (AUB) is an important clinical entity[1]. AUB has a lifetime prevalence of 30% during the reproductive age group[2] that continues until menopause[3]. AUB accounts for 25% of total gynaecological surgeries[4]. In a normal woman, the menstruation is characterized by a frequency of 24-38 days, lasting for 4.5- 8 days, with blood loss ranging between 5-80 ml per cycle[4]. Therefore, variations in any of these four parameters constitute AUB.

In perimenopausal women, AUB is diagnosed when there is a substantial change in frequency, duration and amount of bleeding between periods. In post-menopausal women, any vaginal bleeding one year after cessation of menses is considered abnormal and requires evaluation. Bleeding is said to be abnormal when the pattern is irregular, of abnormal duration or of abnormal amount (>80ml/menses)[5].

AUB has varied presentations like heavy menstrual bleeding, frequent cycles, irregular cycles, post-coital bleeding and post-menopausal bleeding. The Federation of Gynaecology and Obstetrics (FIGO), in 2011, devised a classification named PALM-COEIN for the etiology of AUB. PALM accounts for structural features like polyps, adenomyosis, leiomyoma and malignancy. COEIN advised non-structural causes like coagulation defect, ovulatory dysfunction, endometrial causes, iatrogenic causes and non-classified ones[6].

BCL2 family is the best characterized protein family involved in the regulation of apoptotic cell death, consisting of anti-apoptotic members and pro-apoptotic members. BCL2 family of protein acts as a critical life-death decision point within the common pathway of apoptosis. BCL2 is an anti-apoptotic gene that regulates the mitochondrial membrane[7] . The product of the Bcl-2 (B-cell lymphoma/ leukaemia 2) gene was first identified from the t(14;18) translocation occurring in most cases of follicular lymphoma.[8-10] The t(14;18) translocation juxtaposes the Bcl-2 gene (chromosome 18) with the immunoglobulin heavy chain gene, leading to deregulated expression of Bcl-2. These findings suggest that overexpression of Bcl-2 plays a major role in the occurrence of B-cell malignancies, and that Bcl-2 is a protooncogene. It

has been demonstrated that Bcl-2 can extend the survival of some hematopoietic cell lines and neuronal cells despite growth factor deprivation.[11-13] This effect occurs through the inhibition of apoptosis, i.e. programmed cell death, which is involved in the homeostasis of many tissues.[14-17]

Ki67 is one of the most commonly used biomarker for assessing cell proliferation. Ki67 is a DNA-binding protein that is mainly distributed in the nucleus and is related to cell proliferation. Ki67 is usually distributed in the nucleus, and its main role is to maintain the DNA structure during cell mitosis. The primary structure of Ki67 is not known. Ki67 is absent in quiescent cells (Go). [18-19]

Aim and Objectives

1) To evaluate the clinical and histomorphological spectrum in cases of Abnormal Uterine Bleeding.
2) To study the role of BCl 2 and Ki 67 in cases of Abnormal Uterine Bleeding

2. Material and Methods

The study was conducted at the Department of Pathology, LLRM Medical College, Meerut in collaboration with the Department of Obstetrics and gynaecology, SVBP Hospital, LLRM Medical College, Meerut. The sources of data for the study consisted of endometrial biopsies tissue samples preserved in 10% neutral buffered formalin. These samples were received in the histopathology laboratory and were processed routinely.

Study Design: This study was designed as a prospective cross- sectional study.

Study Place: The study was conducted at the Department of Pathology, Lala Lajpat Rai Memorial Medical College, Meerut.

Study Duration: The study was carried out over a period of one year. This duration included the time for patient recruitment, data collection, laboratory analysis, and data evaluation.

Sample Size: The study included a total of 150 cases

Inclusion Criteria:

- Patients age more than 18 years with history of AUB for a period of 6 months or above.
- Adequate clinical details
- Adequate endometrial specimens received in the form of endometrial curettage and endometrial biopsy.

Exclusion Criteria:

- Patients of AUB due to gestational causes like incomplete abortion, missed abortion and retained products of conception.
- Inadequate clinical details, autolysed tissue and inadequate material, will also be excluded from the study.

Method of Collection of Data

All the patients included in this study were subjected to standard diagnostic criteria, including detailed history, physical examination, histological examination and, subsequently, Immunohistochemical analyses. Written informed consent was obtained from all the patients included in the study.

The results were presented as frequency and percentages.

3. Observations and Results

The present study was done at the Department of Pathology, in collaboration with department of Obstetrics and Gynecology, LLRM medical college, attached to SVBP Hospital, Meerut. A total of 150 cases of endometrial biopsies were studied from June 2023 to May 2024. All cases were distributed in three categories according to their age group.

Table 1: Age group distribution of AUB patients

Age group of AUB patient	Frequency	Percentage (%)
Reproductive (18-40 years)	60	40
Perimenopausal (41-50 years)	76	50.7
Postmenopausal (>50 years)	14	9.3
Total	150	100

Table 1. represents the age group distribution of patients presented with abnormal uterine bleeding . Among the 150 AUB cases, the majority, 50.7% cases (n=76), belonged to the perimenopausal age group (41-50 years). The reproductive age group (18-40 years) accounted for 40% (n=60) of cases, while the postmenopausal group (>50 years) had the least proportion of cases, comprising 9.3% (n=14).

Table 2: Bleeding pattern distribution in AUB patients

Bleeding pattern in AUB patient	Frequency	Percentage (%)
Menorrhagia	101	67.3
Metrorrhagia	26	17.3
Hypomenorrhea	14	9.3
Post-menopausal bleeding	9	6
Total	150	100

Table 2. represents the distribution of different bleeding patterns among patients presented with abnormal uterine bleeding. Among the 150 cases, the most frequently observed bleeding pattern was menorrhagia, affecting 67.3% (n=101) of cases. Metrorrhagia was reported in 17.3% (n=26) of cases, while hypomenorrhea accounted for 9.3% (n=14) of cases. Postmenopausal bleeding, though less common, was seen in 6% (n=9) of cases.

Table 3: Histomorphological spectrum of AUB patients

	Histomorphological diagnosis		Frequency	Percentage (%)
Functional causes (n = 96, 64%)		Proliferative phase	37	24.7
		Disordered proliferative phase	30	20
		Secretory phase	24	16
		Atrophic endometrium	5	3.3
Organic causes (n = 54, 36%)	Benign causes	Endometrial polyp	25	16.7
		Chronic non specific endometritis	8	5.3
		Granulomatous endometritis	2	1.3
	Hyperplasia / Carcinoma	Endometrial hyperplasia without atypia	11	7.3
		Endometrial hyperplasia with atypia	2	1.3
		Endometrial carcinoma	6	4
	Total		150	100

Table 3. represents the histomorphological diagnosis of patients with abnormal uterine bleeding, categorized into functional and organic causes. Among the 150 cases, functional causes were more prevalent, accounting for 64% (n=96) of cases. Within this category, the proliferative phase endometrium was observed in 24.7% (n=37) of cases, while the secretory phase endometrium was identified in 16% (n=24) of patients. Disordered proliferative endometrium, a condition often associated with hormonal imbalances, was found in 20% (n=30) of cases, While atrophic endometrium was seen in a smaller proportion, comprising 3.3% (n=5) of cases. In contrast, organic causes were diagnosed in 36% (n=54) of cases. The most common pathology in this group was endometrial polyp, detected in 16.7% (n=25) of cases. Endometrial hyperplasia without atypia was found in 7.3% (n=11) of cases while endometrial hyperplasia with atypia was observed in 1.3% (n=2) of cases. Among inflammatory conditions, chronic non-specific endometritis was present in 5.3% (n=8) of cases, while granulomatous endometritis was seen in 1.3% (n=2) of patients. Endometrial carcinoma, was identified in 4% (n=6) of cases. This histomorphological analysis of present study showed that functional causes form the majority of AUB cases (64 %), while cases with organic pathology were only 36 %. This emphasises the need for thorough histopathological evaluation in patients presenting with abnormal uterine bleeding.

Table 4: Correlation between Histomorphological diagnosis and BCL-2 expression in AUB patients

	Histomorphological diagnosis		BCL-2 expression		Total No. and %
			Positive No. and %	Negative No. and %	
Functional causes (n = 96, 64%)		Proliferative phase, n (%)	25 (67.6)	12 (32.4)	37 (100)
		Disordered proliferative endometrium, n (%)	5 (16.7)	25 (83.3)	30 (100)
		Secretory phase, n (%)	12 (50)	12 (50)	24 (100)
		Atrophic endometrium, n (%)	0 (0)	5 (100)	5 (100)
	Total Functional causes, n (%)		42 [43.8]	54 [56.2]	96 [100]
Organic causes (n = 54, 36%)	Benign causes	Endometrial polyp, n (%)	7 (28)	18 (72)	25 (100)
		Chronic non- specific endometritis, n (%)	1 (12.5)	7 (87.5)	8 (100)
		Granulomatous endometritis, n (%)	0 (0)	2 (100)	2 (100)
	Hyperplasia/ Carcinoma	Endometrial hyperplasia without atypia, n (%)	4 (36.4)	7 (63.6)	11 (100)
		Endometrial hyperplasia with atypia, n (%)	0 (0)	2 (100)	2 (100)
		Endometrial carcinoma, n (%)	2 (33.3)	4 (66.7)	6 (100)
	Total organic causes, n (%)		14 [25.9]	40 [74.1]	54 [100]
	Grand Total		56	94	150
	Chi-square value = 4.693 p-value = 0.0303 (Significant)				

Table 4 represents the distribution of BCL-2 expression among patients of abnormal uterine bleeding based on histomorphological findings, categorized into functional and organic causes. Among the 150 patients, BCL-2 expression was more commonly observed in functional causes, where 43.8% (n=42) of cases were BCL-2 positive, while 56.2% (n=54) were BCL-2 negative. Within this group, the highest BCL-2 positivity was seen in the proliferative phase endometrium, where 67.6% (n=25) of cases exhibited positive expression, whereas 32.4% cases (n=12) were negative. In the secretory phase, positivity was found in 50% (n=12) of cases, while the remaining 50% cases (n=12) were negative. Disordered proliferative endometrium had a lower positivity rate, with only 16.7% cases (n=5) showing BCL-2 expression, while the majority, 83.3% cases (n=25), were negative. Among organic causes, BCL-2 positivity was significantly lower, with only 25.9% (n=14) of cases showing positive expression, while 74.1% cases (n=40) were negative. Within this category, chronic non-specific endometritis exhibited BCL-2 positivity in only 12.5% (n=1) of cases, while 87.5% cases (n=7) were negative. Granulomatous endometritis and endometrial hyperplasia with atypia showed no BCL-2 positivity, with all cases being negative. Endometrial polyps had a positivity rate of 28% cases (n=7), while 72% cases (n=18) were negative. Endometrial hyperplasia without atypia showed BCL-2 expression in 36.4% (n=4) of cases, while 63.6% (n=7) were negative. Among malignant cases, endometrial carcinoma exhibited BCL-2 positivity in 33.3% (n=2) of cases, whereas 66.7% (n=4) were negative. The chi-square value (4.693) and p-value (0.0303) indicate that the observed difference in BCL-2 expression across different histomorphological diagnoses was statistically significant at the 5% level of significance. This suggests that BCL-2 expression is significantly higher in functional causes, particularly in proliferative phase endometrium, as compared to its expression in organic causes

including hyperplasia, malignancy and inflammatory conditions.

Table 5: Correlation between Histomorphological diagnosis and Ki 67 expression in AUB patients

	Histomorphological diagnosis		Ki 67 expression		Total
			Positive	Negative	
Functional causes (n = 96, 64%)		Proliferative phase, n (%)	16 (43.2)	21 (56.8)	37 (100)
		Disordered proliferative endometrium, n (%)	4 (13.3)	26 (86.7)	30 (100)
		Secretory phase, n (%)	10 (41.7)	14 (58.3)	24 (100)
		Atrophic endometrium, n(%)	0 (0)	5 (100)	5 (100)
	Total Functional causes, n (%)		30 [31.3]	66 [68.7]	96 [100]
Organic causes (n = 54, 36%)	Benign	Endometrial polyp, n (%)	9 (36)	16 (64)	25 (100)
		Chronic non- specific endometritis, n (%)	1 (12.5)	7 (87.5)	8 (100)
		Granulomatous endometritis, n (%)	0 (0)	2 (100)	2 (100)
	Hyperplasia and Carcinoma	Endometrial hyperplasia without atypia, n (%)	10 (90.9)	1 (9.1)	11 (100)
		Endometrial hyperplasia with atypia, n (%)	1 (50)	1 (50)	2(100)
		Endometrial carcinoma, n (%)	4 (66.7)	2 (33.3)	6 (100)
	Total organic causes, n (%)		25 [46.3]	29 [53.7]	54 [100]
	Grand Total		55	95	150
	Chi-square value = 3.37 p-value = 0.0664 (Not significant)				

Table 5 represents the distribution of Ki-67 expression among patients of abnormal uterine bleeding (AUB) based on histomorphological findings, categorized into functional and organic causes. Among the 150 patients, Ki-67 expression was more commonly observed in organic causes, where 46.3% (n=25) of cases were Ki-67 positive, while 53.7% (n=29) were negative. In contrast, functional causes showed lower positivity, with only 31.3% (n=30) exhibiting Ki-67 expression, while the majority, 68.7% (n=66), were negative. Within the functional category, proliferative phase endometrium had a Ki-67 positivity rate of 43.2% (n=16), while 56.8% (n=21) were negative. The secretory phase endometrium exhibited a similar trend, with Ki-67 positivity in 41.7% (n=10) of cases and negativity in 58.3% (n=14). Disordered proliferative endometrium had a much lower Ki-67 expression, with only 13.3% cases (n=4) showing positivity, while 86.7% (n=26) were negative. Atrophic endometrium showed no Ki-67 positivity, with all cases (100%, n=5) were negative. Among organic causes, endometrial hyperplasia without atypia exhibited the highest Ki-67 expression, with 90.9% (n=10) of cases showing positivity, while only 9.1% (n=1) were negative. Endometrial carcinoma showed Ki67 positivity in 66.7% (n=4) of cases showing Ki-67 positivity, while 33.3% cases (n=2) were negative. Endometrial hyperplasia with atypia exhibited Ki-67 positivity in 50% (n=1) of cases, while the remaining 50% (n=1) negative. Endometrial polyps had Ki 67 positivity in 36% cases (n=9) while 64% (n=16) were negative. Chronic non-specific endometritis and granulomatous endometritis showed very low or no Ki-67 expression, with positivity rates of 12.5% (n=1) and 0% (n=0) respectively. The chi-square value (3.37) and p-value (0.0664) indicate that the observed difference in Ki-67 expression across different histomorphological diagnoses was not statistically significant at the 5% level of significance. This suggests that while Ki-67 expression tends to be higher in cases of hyperplasia and malignancy, the association between histomorphological diagnosis and Ki-67 expression is not statistically significant, indicating that additional factors may influence its expression in AUB cases.

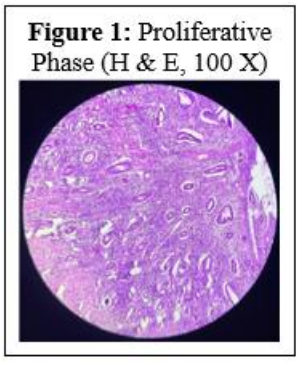


Figure 1: Proliferative Phase (H & E, 100 X)

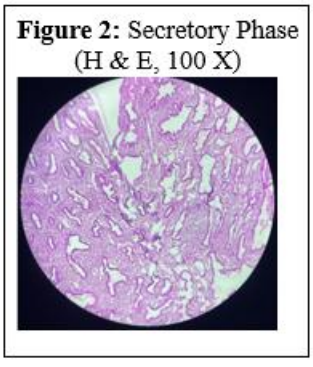


Figure 2: Secretory Phase (H & E, 100 X)

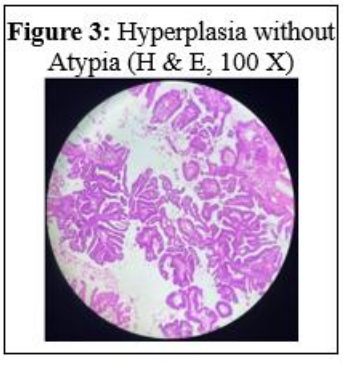


Figure 3: Hyperplasia without Atypia (H & E, 100 X)

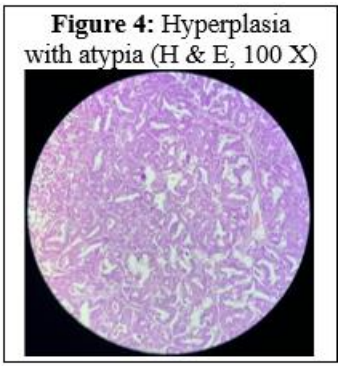


Figure 4: Hyperplasia with atypia (H & E, 100 X)

Figure 5: Endometrial Carcinoma (H & E, 100 X)

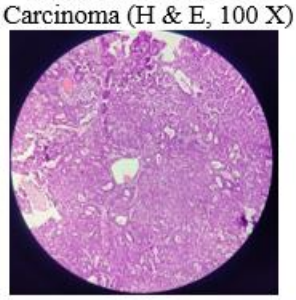


Figure 6: BCL-2 positive in proliferative phase (IHC, 400 X)

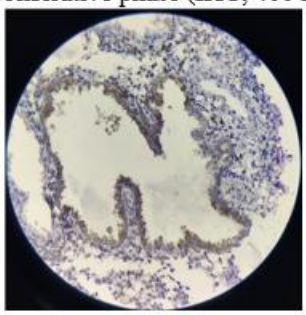
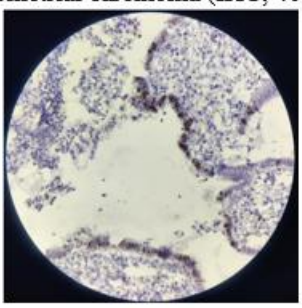


Figure 7: Ki-67 positive in endometrial carcinoma (IHC, 400 X)



4. Discussion

In present study, the highest incidence of AUB was observed in perimenopausal women (50.7%), followed by reproductive-age women (40%) and postmenopausal women (9.3%). This is consistent with studies by Soleymani et al (2014)[20] ,Sinha et al. (2018)[21], Khare et al. (2018)[22] , Muzaffar et al. (2018)[23] ,Behera et al. (2020)[24] ,Chaudhary SA Nath P. et al. (2020)[25] and Sweta et al (2023)[26] who reported that perimenopausal women constitute the largest proportion of AUB cases due to hormonal fluctuations, anovulatory cycles, and declining ovarian function, which leads to unopposed estrogen stimulation[1,2]. However, some studies, such as those by Doraiswami et al. (2011)[27], reported a slightly lower prevalence of AUB in perimenopausal women (45%) and a higher incidence in postmenopausal women (15%)[3]. Deka et al. (2018)[28] reported higher incidence in reproductive age group (34%). The differences in findings could be due to variations in study populations, healthcare-seeking behavior, and referral biases. Additionally, in regions with a higher life expectancy and increased prevalence of metabolic disorders such as obesity and diabetes, postmenopausal AUB cases may be more frequent.

Studies	Doraiswami et al (2011)[27]	Sinha K et al (2018)[21]	Deka et al (2018) [28]	Behera et al (2020)[24]	Choudhary SANath et al (2020)[25]	Present study (2025)
Age group	Perimenopausal (41-50yr) (45%)	Perimenopausal (41-50yr) (58%)	Perimenopausal (41-50yr) (34%)	Perimenopausal (41-50yr) (43.25%	Reproductive (41-50yr) (46%)	Perimenopausal (41-50yr) (50.7%)

The most common bleeding pattern in present study was menorrhagia (67.3%), which aligns with the findings of Chattarsal et al. (2017)[29], Mukhopadhyay et al (2018)[30], Kotagasti et al. (2019)[31], and Dangal et al. (2019)[32], Behera et al (2020)[33], Choudhary SA Nath et al. (2020)[34] where menorrhagia was the predominant symptom in AUB cases. The high prevalence of menorrhagia among different studies is likely due to the hormonal imbalance associated with perimenopause, particularly estrogen dominance without adequate progesterone opposition, leading to excessive endometrial proliferation and irregular shedding. However, the prevalence of metrorrhagia (17.3%) and postmenopausal bleeding (6%) in present study was slightly lower than that reported by Jairajpuri et al. (2020)[35], who found metrorrhagia in 22% and postmenopausal bleeding in 10% of cases. The variation may be attributed to differences in the inclusion criteria, where some studies included more elderly patients or those with endometrial hyperplasia and malignancy, conditions more frequently associated with postmenopausal bleeding.

Studies	Chattarsal et al. (2017)[29]	Sinh K et al (2018)[21]	Mukhopadhyay et al (2018)[30]	Behera et al (2020)[24]	Chaudhary SA Nath et al (2020)[25]	Present study (2025)
Bleeding pattern	Menorrhagia (45.5%)	Menorrhagia (47.7%)	Menorrhagia (53%)	Menorrhagia (57.12%)	Menorrhagia (58.45%)	Menorrhagia (67.3%)

The present study found that functional causes were more common (64%) than organic causes (36%). Among the functional causes, proliferative-phase endometrium (24.7%) was the most common finding, which is consistent with Dangal et al. (2019)[36], who reported similar rates of proliferative-phase endometrium in perimenopausal women. The predominance of functional causes in AUB cases suggests that hormonal dysregulation remains the leading factor in the pathogenesis of AUB. Disordered proliferative endometrium was observed in 20% of cases, which is similar to findings by Abdullah et al. (18%) (2021)[37]. This condition is often associated with chronic estrogen stimulation without progesterone counter action, leading to an irregular endometrial response. The high prevalence of this pattern, as reported among different studies, suggests that many AUB cases result from anovulatory cycles, particularly in perimenopausal women. Among the organic causes, endometrial polyps were the most frequent pathology (16.7%). This aligns with studies by Abdullah et al. (2021)[37], who found a similar frequency of polyps in AUB cases. However, some studies have reported a higher prevalence of endometrial hyperplasia compared to polyps. Study by Chattarsal et al. (2017)[38] reported endometrial hyperplasia (25.3%) and Sajitha et al. (2014)[39] reported hyperplasia (25%) as the most common cause of AUB. In present study, the prevalence of endometrial hyperplasia (8.6%) was slightly lower than that reported by Munro et al. (12%) (2021)[40]. Differences in diagnostic thresholds, histological classification systems, and patient selection criteria may explain this discrepancy. Additionally, variations in environmental and lifestyle factors, such as obesity and hormone therapy use, could influence the frequency of

hyperplasia. Endometrial carcinoma was identified in 4% of cases, which is in agreement with the findings of Jairajpuri et al. (4.5%) (2020)[41]. However, Farquhar et al. (2022)[42] reported a slightly higher incidence (6%). This variation may be due to differences in the demographic composition of study populations, as endometrial carcinoma is more common in older women. Additionally, improved screening techniques in some regions may lead to earlier detection, resulting in higher reported prevalence.

Studies	Bhatta et al. (2012)[53]	Sharma et al. (2018)[54]	Mukhopadhyay et al. (2018)[30]	Behara et al. (2020)[24]	Choudhary SA Nath P. et al (2020)[25]	Present study (2025)
Histomorphological spectrum	Proliferative phase (26.23%)	Proliferative phase (38.8%)	Proliferative phase (43%)	Proliferative phase (38.7%)	Proliferative phase (42%)	Proliferative phase (24.7%)

BCL-2 expression was positive in 37.3% of cases, with the highest expression in functional causes, particularly in the proliferative-phase endometrium (67.6%). This is in agreement with findings by A.Gompel et al (1994)[43], Vaskivuo et al (2000)[44], Mertens H J MM etal et al (2002)[45], Jabbour et al. (2021)[46], who reported that BCL-2 is highly expressed in estrogen-dominant conditions, where it plays a role in preventing apoptosis and promoting endometrial cell survival. However, BCL-2 expression was significantly lower in malignancies (33.3%), which is consistent with research by Shukla et al. (2022)[47], who demonstrated that BCL-2 downregulation is associated with apoptotic activation in endometrial carcinoma. This suggests that BCL-2 may serve as a biomarker to differentiate benign proliferative conditions from malignant transformations.

Ki-67 expression was positive in 36.7% of cases, with the highest positivity in endometrial hyperplasia without atypia (90.9%) and endometrial carcinoma (66.7%). These findings are consistent with studies by Dehghani et al. (2021)[48], who reported that Ki-67 is a strong marker of proliferative activity and is significantly expressed in hyperplastic and malignant endometrial conditions. Study done by Robert et al. (2000)[49] reported Ki-67 had mean index high in hyperplasia without atypia. Morsi, Hassan et al. (2000)[50] showed high expression in hyperplasia without atypia and increased expression as grade of endometrial carcinoma progressed. Olega B. Ioffe et al. (1998)[51] showed Ki-67 index was increased in endometrial carcinoma while decrease in hyperplasia. However, in present study, Ki-67 expression in postmenopausal bleeding cases (66.7%) was higher than in some other studies. Feldman et al. (2021)[52] found lower Ki-67 expression in postmenopausal endometrium unless malignancy was present. The higher Ki-67 expression observed in postmenopausal cases in present study may be due to the inclusion of a higher proportion of premalignant lesions, which exhibit increased cellular proliferation.

Studies	A.Gompel et al(1994)[43]	Olga B. Ioff et al(1998)[51]	Robert et al(2000)[49]	Vaskivuo et al (2000)[44]	Morsi Hassan et al(2000)[50]	Mertens HJMM etal (2002)[45]	Present Study (2025)
BCL-2 expression	Increased in proliferative phase, disappeared in secretory phase	Decrease in hyperplasia and carcinoma	-	Increased in proliferative phase, decreased in secretory phase	High in hyperplasia without atypia, weak in endometrial carcinoma	Increased in proliferative phase, decreased in secretory phase	High in proliferative phase
Ki-67 expression		Increase in carcinoma	Lower expression in hyperplasia with atypia than in without atypia	Increased in proliferative phase, decreased in secretory phase	Increased expression in endometrial carcinoma and hyperplasia without atypia	Increased in proliferative phase, decreased in secretory phase	High in hyperplasia without atypia and endometrial cacinoma

5. Conclusion

Abnormal uterine bleeding (AUB) is a common gynecological complaint affecting women of all age groups, with causes ranging from hormonal imbalances to organic pathologies such as endometrial hyperplasia and malignancy. Histopathological examination plays a crucial role in diagnosing AUB, while immunohistochemical markers like BCL-2 and Ki-67 provide additional insights into endometrial cell proliferation and apoptosis. The highest incidence of AUB was observed in perimenopausal women followed by reproductive-age women and postmenopausal women. Menorrhagia was the most common bleeding pattern. Functional causes were more prevalent than organic causes, with proliferative-phase endometrium and disordered proliferative endometrium being the most frequently observed histopathological patterns. Endometrial polyp and hyperplasia were the leading organic causes. Endometrial carcinoma was primarily observed in post- menopausal women, so there is need for careful evaluation in this age group.

Immunohistochemical analysis showed BCL-2 positivity predominantly in functional causes such as proliferative-phase endometrium and secretory-phase endometrium. Lower BCL-2 expression was observed in endometrial malignancies, indicating its potential role in apoptotic regulation. Ki-67 expression was high in endometrial hyperplasia and endometrial carcinoma, suggesting its strong association with cellular proliferation. These findings suggest BCl-2 and Ki-67 can be used as useful marker in identifying high risk cases and differentiating benign from malignant conditions.

6. Recommendations

All women presenting with abnormal uterine bleeding, especially in the perimenopausal and postmenopausal age

groups, should undergo endometrial sampling for histopathological evaluation. Early identification of functional versus organic causes is essential to guide timely management. Routine use of immunohistochemistry in suspicious cases can aid in detecting premalignant and malignant lesions.

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Conflicts of interest
There are no conflicts of interest.

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