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Original Article

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Abnormal Uterine Bleeding: Histopathological Patterns of Endometrium in Elderly Women

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Abstract

Objective: To evaluate endometrial histopathological patterns and observe their frequency in elderly women presenting with abnormal uterine bleeding. ***Design:*** Retrospective observational study. ***Subjects/Patients:*** 200 women aged over 40 years presenting with Abnormal Uterine Bleeding between 2017 and 2019. ***Methods:*** Endometrial samples from dilatation and curettage and hysterectomy specimens were fixed in 10% formalin, processed into paraffin blocks, stained with Haematoxylin and Eosin, and evaluated for histological patterns. ***Results:*** The maximum number of cases occurred in the fifth decade (57%). Menorrhagia was the most common clinical presentation (54%). Histopathologically, the proliferative pattern was the most frequent ovulatory finding (32.5%). Among anovulatory causes, simple endometrial hyperplasia without atypia was most common (27%). Endometrial carcinoma was identified in 1.5% of cases, primarily in the 61–65 age group. ***Conclusion:*** Histopathological evaluation of the endometrium is essential in perimenopausal and postmenopausal women with AUB to identify precise underlying causes and exclude malignancy.

Keywords: ***Abnormal Uterine Bleeding; Endometrial Hyperplasia; Histopathology; Menorrhagia.***

Introduction

Abnormal uterine bleeding (AUB) is the commonest presenting symptom and major perplexing gynaecological problem responsible for as many as one-third of all out patient gynaecologic visit [1,2].

Variations from the normal cyclical pattern in the peri-menopausal age may be due to physiological hormonal changes or may be due to neoplastic changes [3].

Abnormal uterine bleeding is defined as any bleeding pattern that differs in the frequency, duration and amount from a pattern observed during a normal menstrual cycle or menopause [4].

Heavy menses, prolonged menses or frequent irregular bleeding are the most common complaints. AUB is a symptom and not a disease that occurs in different patterns [5,6].

AUB is the commonest cause of iron deficiency anaemia in the developed countries and the chronic illness in developing world[7].

AUB may be the symptom of endometrial carcinoma in 8-50% of cases [8].

The increased risk of endometrial hyperplasia and endometrial carcinoma is more evident in perimenopausal and post-menopausal women with abnormal uterine bleeding [9].

Postmenopausal bleeding (PMB) is defined as that uterine bleeding which occurs after 12 months of the last menstrual period. It is an important symptom which requires careful and prompt evaluation, because it may be a symptom of endometrial neoplasia[10-12].

The hormonal assay is very expensive and laboratories with hormonal assay are not available in rural areas [13]. Ultrasonography (USG), hysteroscopy and hysterosalpingography are mainly helpful in diagnosing organic pathology except in endometrial atrophy and hyperplasia [14]. So, endometrial specimen examination by histopathological evaluation is relatively inexpensive, accurate and a gold standard procedure to know the exact pathology for AUB.

Methods

The present study was conducted in the Department of Pathology between 2017 and 2019. Detailed clinical history was collected from the patients along with relevant investigations as per the requisition form.

Inclusion criteria: The cases of abnormal uterine bleeding attending the gynaecology OPD with complaints of menorrhagia, metrorrhagia, polymenorrhoea, polymenorrhagia in the age group more than 40 years women.

Exclusion criteria: Women of ≤ 40 years of age or women with pregnancy complications, acute pelvic inflammatory disease, abnormal cervical pap smear, previous abnormal endometrial biopsy, leiomyoma, haemostatic disorders were excluded.

The endometrial samples (D & C and hysterectomy specimens) sent to pathology laboratory were analysed. These specimens were fixed in 10% formalin and gross morphology were recorded. Endometrial samples were totally embedded and representative bits were taken from hysterectomy specimens. These bits were placed in cassettes and kept in fixative and processed in the tissue processor. Paraffin tissue blocks were prepared and 3-4 micrometre thick sections were cut and stained with routine haematoxylin and eosin. A detailed

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histological study was carried out and the findings were noted. Statistical analysis was done using Microsoft excel software.

Results

Results are depicted in tabular form in Table I to Table V.

A total of 200 cases were included in this study.

Hysterectomy specimens (64%) were the most common sample type. Most patients were multiparous (74%).

Age: 57% of patients were in the 41–45 age group.

Clinical Presentation: Menorrhagia predominated (54%), followed by metrorrhagia (18%) and postmenopausal bleeding (11%).

Histopathology: Proliferative pattern (32.5%) and simple hyperplasia without atypia (27%) were the leading diagnoses. Malignancy was rare, with endometrial carcinoma found in only 1.5% of cases.

Histopathological images of cases taken into account in this study are given as Figure 1 to Figure 10.

Table I: Frequency of Histopathological Patterns

Histopathological patterns	Patients	Percentage
Proliferative	65	32.5%
Secretory	25	12.5%
Atrophic	08	4.0%
Chronic endometritis	06	3.0%
Progestational effect	13	6.5%
Endometrial polyp	07	3.5%
Simple hyperplasia without atypia	54	27%
Complex hyperplasia without atypia	09	4.5%
Simple hyperplasia with atypia	04	2.0%
Complex hyperplasia with atypia	01	0.5%
Endometrial carcinoma	03	1.5%
Inconclusive	05	2.5%
Total	200	100%

Table II: Age distribution pattern in AUB

Age in years	Patients	Percentage
41-45	114	57%
46-50	54	27%
51-55	13	6.5%
56-60	11	5.5%
61-65	06	3.0%
66-70	02	1.0%
Total	200	100%

Table III: Bleeding patterns in AUB patients

Bleeding pattern	Patients	Percentage
Menorrhagia	108	54%
Metrorrhagia	22	18%
Post menopausal bleeding	36	11%
Polymenorrhagia	19	9.5%
Polymenorrhoea	15	7.5%
Total	200	100%

Table IV: Relationship of AUB with parity

Parity of woman	Patients	Percentage
Multipara	148	74%
Primipara	34	17%
Nullipara	18	09%
Total	200	100%

Table V: Frequency of histopathological patterns in AUB in endometrial specimens by D&C or hysterectomy

Histopathological Patterns	Patients	Percentage
Proliferative	65	32.5%
Secretory	25	12.5%
Atrophic	08	4.0%
Chronic endometritis	06	3.0%
Progestational effect	13	6.5%
Endometrial polyp	07	3.5%
Simple hyperplasia without atypia	54	27%
Complex hyperplasia without atypia	09	4.5%
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Endometrial carcinoma	03	1.5%
Inconclusive	05	2.5%
Total	200	100%

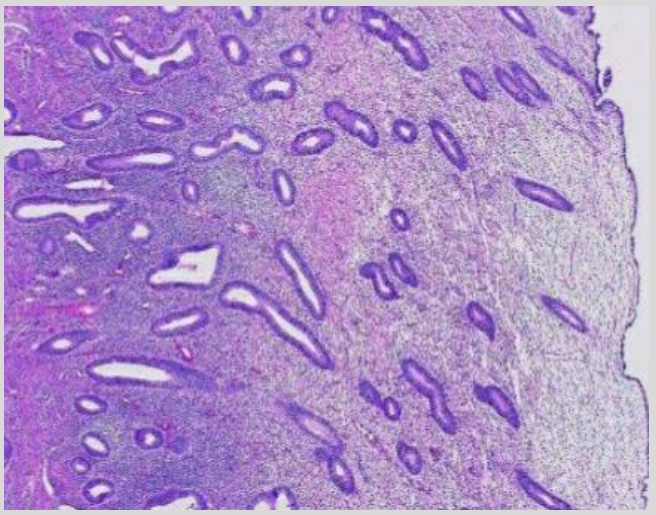

Figure 1: Proliferative phase with round to tubular glands lined by pseudostratified epithelium surrounded by compact stroma. (10x, H&E stain)

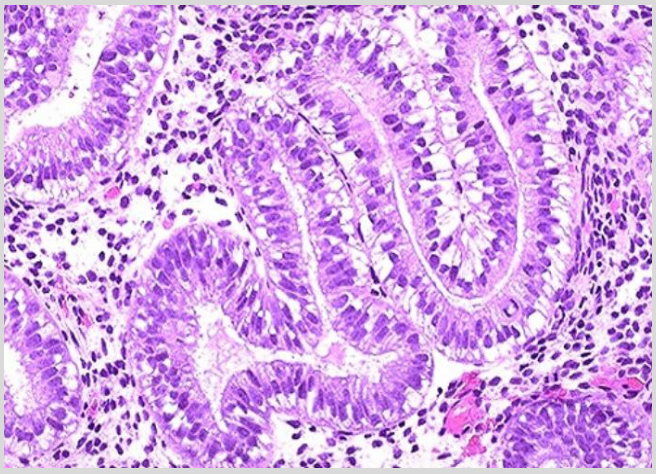

Figure 2: Secretory phase showing subnuclear vacuolations and oedematous stroma. (40x, H&E stain)

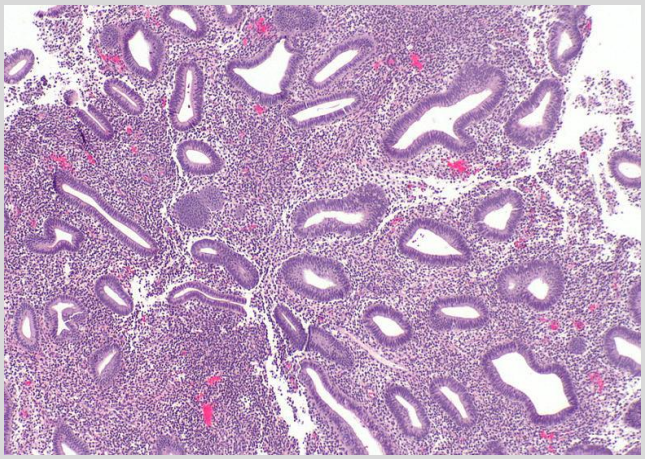

Figure 3: Disordered proliferative pattern showing glandular proliferation with gland to stroma ratio is <3:1. (10x, H&E stain)

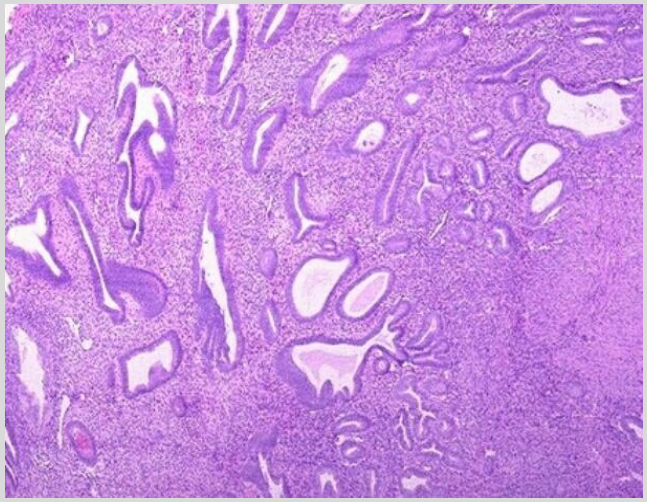

Figure 4: Simple cystic hyperplasia without atypia with variable sized and large cystically dilated glands against compact stroma. (10x, H&E stain)

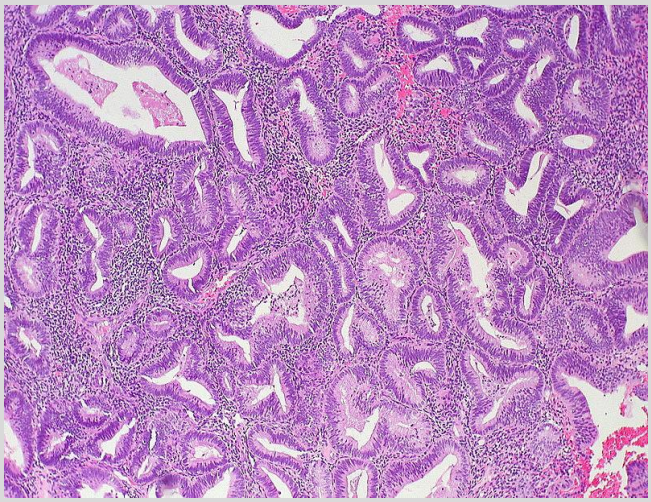

Figure 5: Complex endometrial hyperplasia without atypia showing complex architecture with glandular budding having glands to stroma ratio >3:1. (10x, H&E stain)

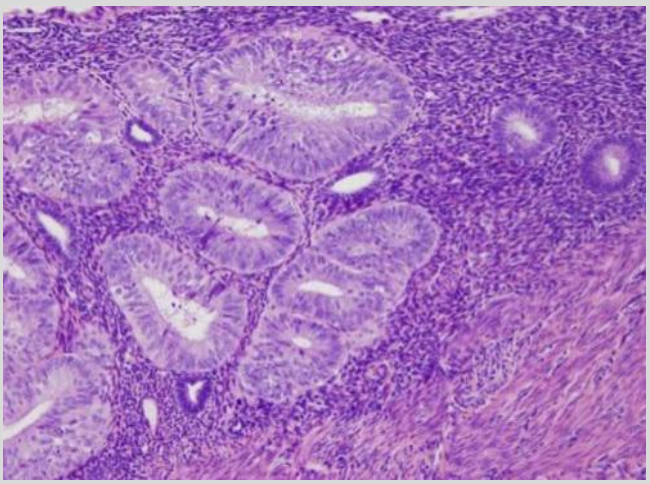

Figure 6: Complex endometrial hyperplasia with atypia showing complex architecture with loss of nuclear polarity, nuclear atypia and high N:C ratio, having glands to stroma ratio >3:1. (40x, H&E stain)

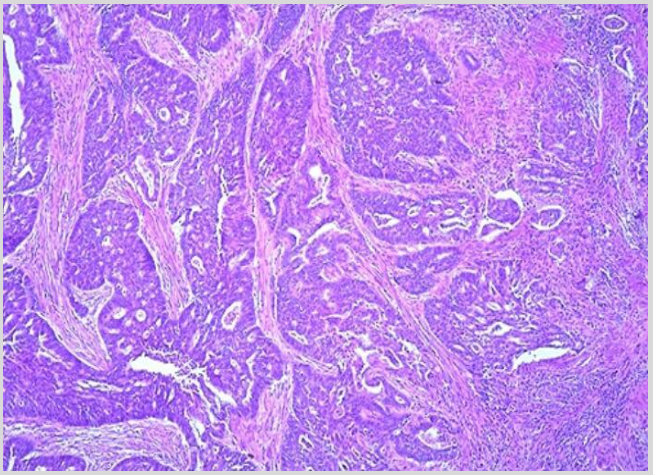

Figure 7: Endometrial carcinoma showing invasion of neoplastic glands in myometrium. (10x, H&E stain)

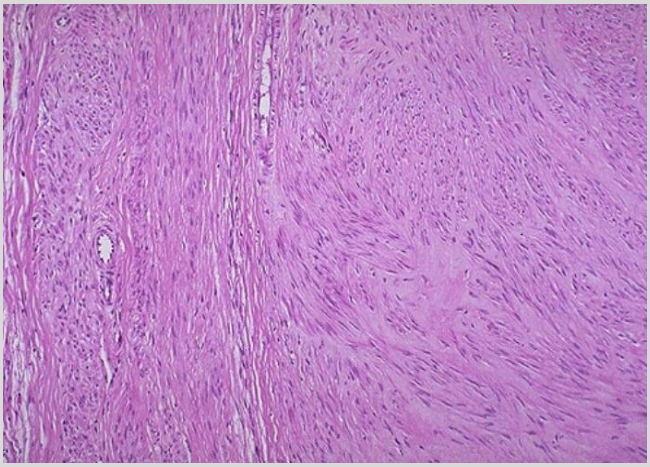

Figure 8: Leiomyoma showing interlacing bundles of smooth muscle fibre and whorl formation. (10x, H&E stain)

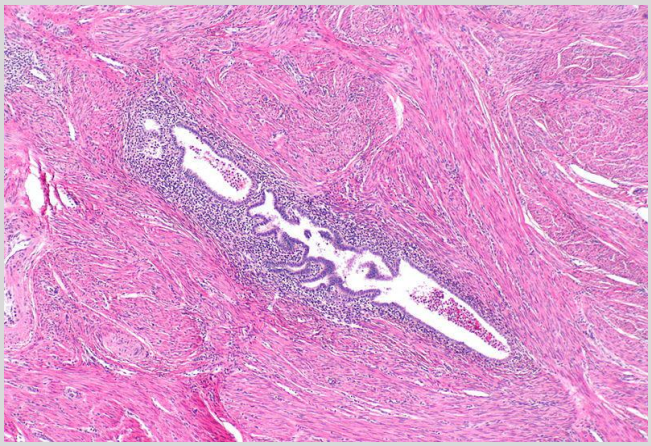

Figure 9: Adenomyosis showing the presence of endometrial glands and stroma in the myometrium. (10x, H&E stain)

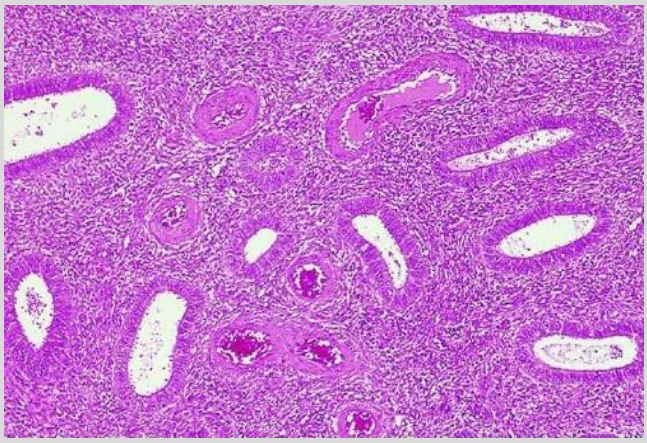

Figure 10: Endometrial polyp showing cystically dilated glands and a fibrous stroma with thick walled vessels. (10x, H&E stain)

Discussion

Abnormal uterine bleeding is one of the most common and challenging problems presenting s an enigma to the gynecologist regardless of the age of the women.

In women of childbearing age, a methodical history, physical examination, and laboratory evaluation may enable the physician to rule out causes such as pregnancy and pregnancy-related disorders, medications, iatrogenic causes, systemic conditions, and obvious genital tract pathology. Dysfunctional uterine bleeding (anovulatory or ovulatory) is diagnosed by exclusion of these causes.

In women of childbearing age who are at high risk for endometrial cancer (obese, diabetic, with cycle irregularity, and diagnosed to have polycystic ovarian disease), the initial evaluation includes endometrial biopsy; saline-infusion sonohysterography or diagnostic hysteroscopy. Women of childbearing age who are at low risk for endometrial cancer may be assessed initially by transvaginal ultrasonography [15].

Postmenopausal women with abnormal uterine bleeding should be offered dilatation and curettage; if they are poor candidates for general anesthesia. If they decline dilatation and curettage, they may be offered transvaginal ultrasonography or saline-infusion sonohysterography with directed endometrial biopsy; not only to identify cause of abnormal uterine bleeding, but also to exclude malignancy.

The findings of the Institute for Social and Economic Change (ISEC) survey done on samples from 1,00,000 women in the age band of 15-50 years, across 26 states highlights that, on an average nearly 4% of Indian women are already menopausal between the ages of 29-34 years.

It goes up to 8 % in the case of women between 35 and 39 years. This is shocking because normal menopause starts between the ages of 45 and 55, with a mean age of around 51 years worldwide. According to the study by ISEC, a higher number of illiterate women experience premature menopause, as against those who are educated and it is slightly more common in women residing rural areas than urban areas [16].

The higher percentage of AUB patients observed in the 5th decade, which is comparable with the other studies. (**Table VI**) Now a days, because of increased awareness amongst patients as well as due to availability of better evaluation techniques, the patients can be evaluated much earlier and treated appropriately. Hence, increased number of perimenopausal patients with AUB is observed in the present study rather than postmenopausal patients.

Table VI: Comparison of age distribution pattern in AUB with other studies

Age in years	Present study	Supriya *et al.*[17] (n=162)	MOH aseel *et al*[18] (n=525)	Rajesh *et al.*[19] (n=190)
41-50	84%	76.72%	71.30%	84.47%
51-60	12%	13.83%	20.38%	15.4%
>60	4%	9.43%	8.30%	-

The reason for increased proportion of abnormal uterine bleeding in the age group 41-50 years may be also because these patients are in their climacteric period. As women approach menopause, cycles shorten and often become intermittently anovulatory due to a decline in the number of ovarian follicles and the estradiol level [20].

Like the present study, menorrhagia is the most commonest type of bleeding pattern in the studies of, Rajesh *et al*.[19], Usha *et al*.[21] and Rajuta *et al*.[22]. (**Table VII**) It is due to the defect in the control process regulating the volume loss during menstrual break down of endometrium which in turn leads to regular episodes of heavy menstrual blood loss.

Table VII: Comparison of bleeding patterns in AUB with other studies

Bleeding pattern	Present study (n=200)	Rajesh *et al.*[19] (n=190)	Usha *et al.*[21] (n=85)	Rujuta *et al.*[22] (n=203)
Menorrhagia	54%	73.16%	45.8%	50.25%
Metrorrhagia	18%	8.4%	28.2%	22.16%
Post menopausal bleeding	11%	-	5.8%	1.49%
Polymenorrhagia	9.5%	7.37%	20.0%	6.40%
Polymenorrhoea	7.5%	6.31%	-	13.79%
Menometrorrhgia	-	4.74%	-	-
Continuous bleeding p/v	-	-	-	5.91%

In our study postmenopausal bleeding pattern is higher than other studies. This might be due to variation of age group selection in different studies.

The percentage of AUB patients was found to be highest in multiparous women and lowest in nulliparous women who are in concordance with the results of the studies by Rajesh *et al.*[19], Usha *et al.*[21] and Sadia khan *et al.*[15] (**Table VIII**).

Table VIII: Comparison of Relationship of AUB with parity in different studies

Parity	Present study (n=200)	Rajesh *et al.*[19] (n=190)	Usha *et al.*[21] (n=85)	Sadiya khan *et al.*[15] (n=500)
Multipara	74%	85.79%	86%	76.2%
Primipara	17%	9.74%	8.2%	18.4%
Nullipara	09%	4.74%	5.8%	5.4%

Proliferative pattern is the most frequently observed pattern amongst all the functional causes of AUB in the present study. The incident of 32.5% of proliferative endometrium compares favorably with that of 37% by Dhanraj *et al.*[23] ,27.8% by Swati *et al.*[24] & 38.1% by Rupal *et al.*[25] but contradicts with higher incidence of 46.6% by Sadia khan *et al.*[15] & lower incidence of 24% by Falguni *et al.*[26], this may be due to selection criteria and timing of D&C. The incidence of 12.5% secretory pattern corresponds with 9.1% by Rupal *et al.*[25] & 13.5% by Falguni *et al.*[26] (**Table IX**).

Table IX: Comparison of Histopathological findings of AUB with other studies.

Histopathological pattern	Present study (n=200)	Dhanra j *et al.*[23] (n=200)	Sadiya khan *et al.*[15] (n=500)	Swati *et al.*[24] (n=212)	Rupal et al[25] (n=380)	Falguni *et al.*[26] (n=200)
Proliferative pattern	32.5%	37%	46.6%	27.8%	38.1%	24%
Secretory pattern	12.5%	31%	38.4%	6.1%	9.1	13.5%
Progestational effect	6.5%	-	-	-	-	4%
Disordered proliferative endometrium	-	-	-	13.7%	-	1%
Deficient secretory phase	-	-	-	3.3%	-	
Atrophic pattern	4%	-	1%	13.2%	1.1	4.5%
Menstrual phase	-	7%	-	-	-	-
Mixed phase	-	2%	-	-	-	-
Simple hyperplasia without atypia	27%	8%	6.4%	15.6%	35.3	7.5%
Simple hyperplasia with atypia	2%	1%	2.4%	1.4%	1.6	-
Complex hyperplasia without atypia	4.5%	1.5%	2.8%	4.7%	2.9	-
Complex hyperplasia with atypia	0.5%	4%	1%	0.5%	3.1	1%
Endometrial polyp	3.5%	0.5%	0.6%	8%	2.6	4.5%
Chronic endometritis	3%	2%	-	2.4%	2.6	-
Endometrial carcinoma	1.5%	-	0.4%	2.3%	0.3	1.5%
Inconclusive	2.5%	6%	-	-	1.1	-
Others	-	-	-	1%	2.1	38.5%

Simple hyperplasia was found 29%, making it the 2nd most common pattern in present study. This might be due to increased awareness in the women leading to early diagnosis at the stage of simple hyperplasia amongst the spectrum of hyperplastic endometrial changes. Other study also reported simple hyperplasia as 2nd most common pattern though the prevalence varies from 7.5% by Falguni *et al.*[26] to 36.9% by Rupal *et al.*[25].

Amongst the anovulatory causes in present study, atrophic pattern showed 4% of cases, which is comparable to 4.5% by Falguni *et al.*[26]. In atrophic endometrium, the thin walled veins, superficial to the expanding cystic glands, make the vessels vulnerable to injury and lead to excessive uterine bleeding [27].

Complex hyperplasia without atypia in our study was observed in 4.5% and with atypia in 0.5% which is comparable to study by. Swati *et al.*[24]

Endometrial carcinoma was found in 1.5% in our study which is comparable to study by Falguni *et al.*[26] 1.5 % & Swati *et al.*[24] 2.3%. A study done by Dangal *et al.*[1] in Nepal documented a lower incidence of endometrial cancer in Nepalese woman attributing it to the practice of early childbearing and multiparity.

This study confirms that AUB predominantly affects women in their fifth decade, likely due to climacteric hormonal fluctuations and a decline in ovarian follicles. Our finding that menorrhagia is the most common symptom (54%) aligns with various studies by Rajesh *et al.*[19] and Rujuta *et al.*[22]. While functional ovulatory causes (proliferative pattern) were common in the 41–65 age group, atrophic patterns became the principle cause in patients over 60. The low incidence of endometrial carcinoma (1.5%) matches observations in other rural and high-parity populations, but its presence emphasizes the need for thorough evaluation in elderly patients.

Conclusion

In conclusion, histopathological pattern of the endometrium varies significantly regardless of age or parity. It remains a valuable diagnostic tool for guiding clinical management and early detection of pre-malignant lesions.

Declarations

Conflict of interest

The authors have no conflicts of interest to declare.

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