

Histomorphological spectrum of endometrial lesion in women presenting with abnormal uterine bleeding: A 3-year study at a tertiary care center

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Abstract

Introduction: Abnormal uterine bleeding (AUB) is the most common presentation amongst the women of all age groups attending the gynecology Out Patient Department. Histopathological evaluation of the endometrial samples plays a significant role in the diagnosis of abnormal uterine bleeding. **Aim:** To determine the various histomorphological patterns of the endometrium in women presenting with AUB. **Material and Method:** A retrospective analysis of 183 patients age ranged from 15 to 71 years, presenting with AUB was done who underwent endometrial sampling during a 3-year period from August 2015 to July 2018 in Department of Pathology at T.S Misra Medical College and hospital. Detailed clinical history like age, menstrual status including painful bleeding, heavy menstrual bleeding, periodicity & regularity of cycle were obtained from the case records. Patients were categorized into reproductive age group, perimenopausal and postmenopausal. Specimens were routinely processed and stained with Haematoxylin& Eosin stain and microscopic morphological evaluation was done. **Results:** The most common age group affected is perimnopausal presenting with AUB frequently seen in 41-50 years of age group (47.5%). The commonest Histomorphological pattern in these patients was proliferative endometrium (38.8%), secretory endometrium (16.3%), endometrial hyperplasia seen in 22 cases (12.0%), hormonal changes/Pill endometrium were seen in 6.0% of the cases and least number cases were of endometrial carcinoma forming 1.1% of the total cases taken in the study. **Conclusion:** In our study patients with AUB show variable pathology on endometrial biopsy as milder as inflammatory cause to as notorious as malignancy.

Key words: Endometrium, Postmenopausal, Malignancy, Abnormal uterine bleeding

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Introduction

Abnormal uterine bleeding (AUB) is the most common presentation amongst the women of all age groups attending the Gynecology Out Patient Department. AUB is the term used to describe any departure from normal menstruation or from a normal menstrual cycle pattern. The key characteristics are regularity, frequency, heaviness of flow and duration of flow [1]. Menstrual bleeding is considered abnormal when the pattern is irregular or prolonged duration (i.e.>20 days) in individual cycle lengths over a period of 1 year or heavy menstrual bleeding. Recently, the International Federation of Gynecology and Obstetrics working group on menstrual disorder has developed a

classification system (PALM-COEIN) for causes of the AUB in non-gravid women of reproductive age. There are nine main categories, which are arranged according to the acronym PALM-COEIN: Polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometritis; iatrogenic; and not yet classified [2]. Two types of causes including functional causes like normal cyclical endometrium, abnormal physiological changes of endometrium (atrophic endometrium, weakly proliferative and disordered proliferative endometrium) and organic lesions like chronic endometritis, endometrial hyperplasia, endometrial polyp, carcinomas and pregnancy related complications [2]. In reproductive age group heavy menstrual bleeding accounts for 30% of total DUB cases [3], while postmenopausal bleeding.

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accounts for 5% of all gynaecological visits. Histopathological examination of endometrial sample is used for the diagnosis of majority of lesions. Endometrial biopsy and curettage are chief sampling methods [4].

Materials and Methods

A retrospective study was undertaken which included 183 endometrial samples with a clinical diagnosis of AUB.

The study was carried out in the Department of Pathology, T.S. Misra Medical College & Hospital Lucknow (U.P.), India, over a period of 3 years from August 2015 to July 2018.

Inclusion Criteria: Patients with isolated endometrial causes of abnormal uterine bleeding were included for study. Endometrial samples (Biopsy or Dilation & Curettage) obtained from those patients were studied.

Results

During the study period of 3 years, a total of 183 endometrial samples were selected.

Table-1 (a): Distribution according to various age groups

Age group (Years)	Number of patients (%)
15-20	06 (3.3%)
21-30	25 (13.7%)
31-40	46 (25.1%)
41-50	87 (47.5%)
51-60	11 (6.1%)
61-70	05 (2.7%)
>70	03 (1.6%)

Table-1(b): Cases in different age groups

Age Group	Cases
Reproductive	77(42.1%)
Perimenopausal	87(47.5%)
Postmenopausal	19 (10.4%)
Total	183

Minimum age of presentation of AUB was 15 years and maximum was 71 years. Most common age group affected was between 4th and 5th decade which is perimenopausal age group (47.5%), (Table 1a & 1b).

Table No-2: Relationship of AUB with bleeding pattern

Bleeding Pattern	No. of Patients(%)
Disturbances of Regularity	30(16.4%)
Disturbances of frequency	28(15.3%)
Disturbances of heaviness of flow	76 (41.5%)
Disturbances of the duration of flow	15(8.2%)
Abnormal bleeding with hormonaltherapy	13(7.1%)
Irregular Non-menstrual bleeding	10(5.5%)
Bleeding outside reproductive age	11(6.0%)

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Table 2 shows that disturbances of heaviness of flow was the commonest bleeding pattern seen in 76 patients (41.5%) followed by disturbances of regularity of menstrual cycle seen in 30 patients (16.4%). Least common bleeding pattern was irregular non- menstrual bleeding seen in 10 patients (5.5%).

Table-3: According to Endometrial Histopathology report.

S. No.	Histomorphology finding	Cases	Percentage %
1.	Proliferative Endometrium	71	38.8%
2.	Secretory Endometrium	30	16.4%
3.	Endometrial Hyperplasia	22	12.0%
4.	Disordered Proliferative Endometrium	12	6.5%
5.	Hormonal change/pill endometrium	11	6.0%
6.	Inadequate	11	6.0%
7.	Atrophic Endometrium	08	4.4%
8.	Pregnancy related changes	06	3.3%
9.	Endometritis	06	3.3%
10.	Endometrial Polyp	04	2.2%
11.	Endometrial Carcinoma	02	1.1%

After detailed microscopic examination, depending upon their histomorphological features all the cases were categorized into 11 groups (Table 3). Amongst these, maximum number of the samples showed proliferative phase 71(38.8%), followed by 30 cases (16.4%) of secretory phase and endometrial hyperplasia 22(12%).

Disordered proliferative endometrium was observed in 12 (6.5%) cases. Hormonal changes/ pill endometrium was observed in 11 cases (6.0%). Total 8 cases (4.4%) revealed atrophic endometrium. Both pregnancy related changes and endometritis were reported in 6 cases (3.3%) each.

Among pregnancy related changes there were 2 cases of retained product of conception (RPOC) and partial mole and single case of complete mole and Arias – Stella reaction each.

Endometritis was seen in 6(3.3%) cases, out of which 1 case showed necrotizing granulomatous endometritis with cystic change i.e caseating granulomas, Langhans type of giant cells, areas of necrosis with cystic dilation of glands. 3 cases showed acute on chronic endometritis & remaining 2 cases show chronic endometritis (Fig 1a & 1b).

Endometrial polyps were seen in 4 (2.2%) cases, out of which 2 cases showed hyperplastic endometrial polyp. Endometrial carcinoma which is common in postmenopausal women was encountered in 2(1.1%) cases.

Scant endometrial tissue with predominantly blood clot, autolyzed samples and tissue with suboptimal fixation that hindered the microscopic evaluation were considered inadequate. In our study 11 samples (6.2%) were inadequate for evaluation and were excluded from the study group.

Table-4: Percentage of Endometrial hyperplasia cases

S.No.	Histologic types	Number cases	Percentage (%)
1	Simple hyperplasia without atypia	12	54.5%
2	Complex hyperplasia without atypia	05	22.7%
3	Simple hyperplasia with atypia	03	13.6%
4	Complex hyperplasia with atypia	02	9.2%

More than half of the histomorphologically reported cases of endometrial hyperplasia showed simple hyperplasia without atypia among which few showed cystic changes. 3 cases (13.6%) showed simple hyperplasia with atypia and whereas 5 (22.7%) cases showed complex hyperplasia without atypia and 2 (9.1%) cases showed complex hyperplasia with atypia (Table 4).

Table-5: Distribution of cases according to different age group.

Age Groups	15-20	21-30	31-40	41-50	51-60	61-70	>70
Proliferative endometrium	02	09	14	45	01	-	-
SecretoryEndometrium	01	07	11	11	-	-	-
EndometriumHyperplasia	-	01	06	13	02	-	-
Disordered ProliferativeEndometrium	-	01	05	04	02	-	-
Hormonal/Pill endometrium	-	01	03	05	01	01	-
Atrophic	-	-	-	02	02	01	03
Inadequate	-	01	03	05	01	01	
PregnancyChange	02	03	01	-	-	-	-
Endometritis	-	02	01	02	-	01	-
Endometrial polyp	01	-	02	-	01	-	-
Endo Ca	-	-	-	-	01	01	-
Total	06	25	46	87	11	05	03

Maximum number of proliferative endometrium, endometrial hyperplasia and pill endometrium were present in the 5th decade. Maximum number of cases of disordered proliferative endometrium in 4th and 5th decades. Endometrial carcinoma was observed in 6th & 7th decade of life (Table 5), (Fig 2&4).

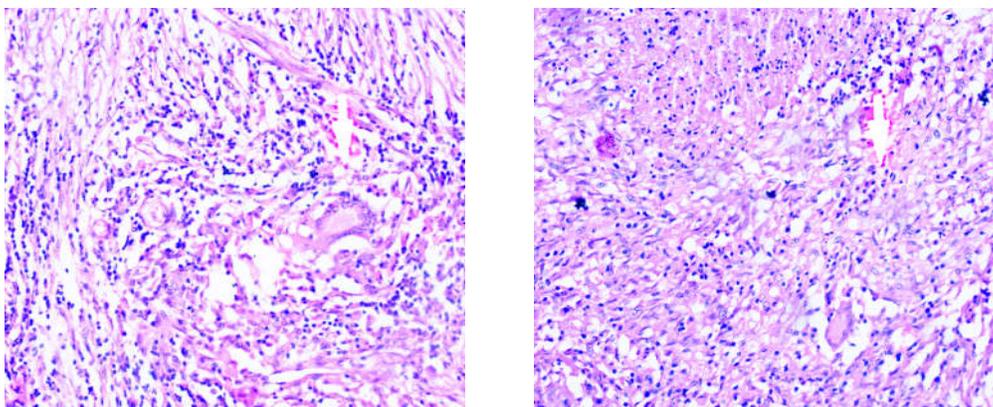


Fig-1a & 1b: Photomicrograph of Necrotizing Granulomatous Endometritis showing Caseating granulomas, Langhans type of giant cells & areas of necrosis (40x & 4x).

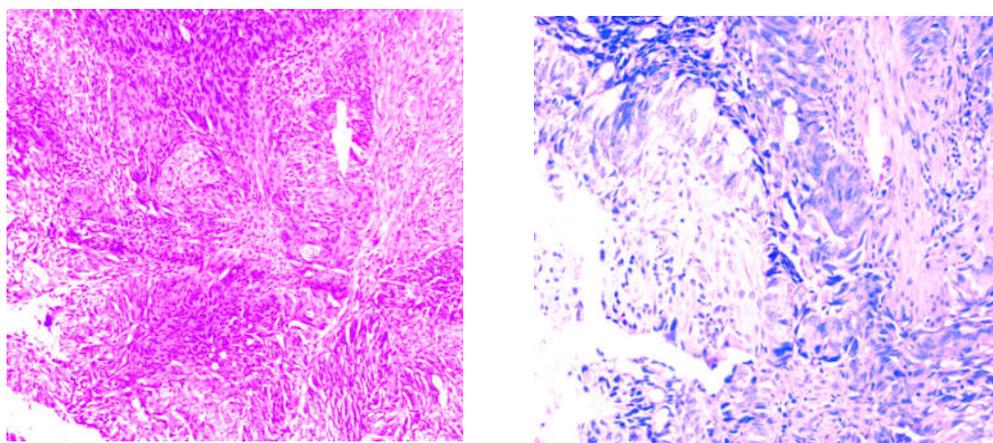


Fig 2a & 2b: Photomicrograph of Endometrial Carcinoma showing invasive complex endometrial gland with anaplastic epithelial cells and pleomorphic hyperchromatic nuclei (10x and 40x)

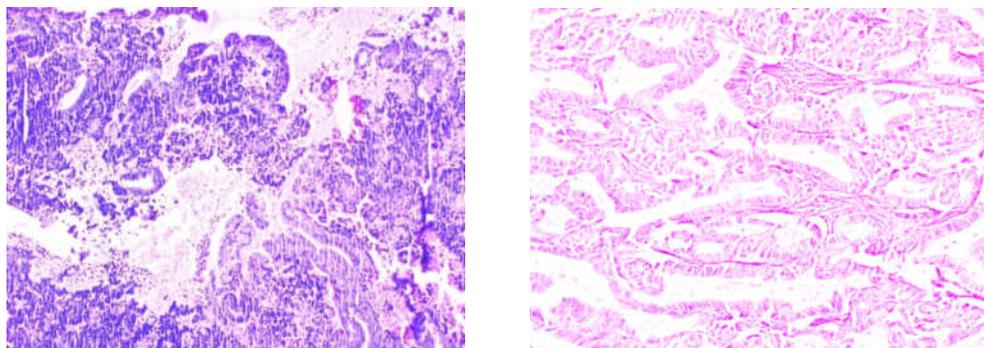


Fig-3: Complex Hyperplasia with atypia (4x), Fig 4: Endometrial Ca with anaplastic back-to-back glands. (40 x)
Table-6: Comparison of various histopathological patterns of endometrium in AUB by various authors

Endometrial Pattern	Present Study	Ayesha Fatima [10] (2017)	Sarika [5] Et al (2016)	AnuradhaSalvi [13] et al (2015)	Rajesh Patil [8] (2013)	BhoomikaDadhiana [14] (2013)
Proliferative	71(38.8%)	56(19.7%)	84(41.6%)	93(37.2%)	42(22.1%)	32(21.3%)
Secretory	30(16.3%)	29(10.2%)	35 (17.3%)	46 (18.4%)	37(19.5%)	23(15.3%)
Hyperplasia	22(12.0%)	132(46.5%)	31(15.3%)	63(25.2%)	76(40%)	40(26.7%)
Disorder Proliferative	12(6.5%)	14(4.93%)	15(7.4%)	-	-	Irregular proliferative 4(2.7%)
Pill/Hormonal Change	11(6.0%)	-	13(6.4%)	-	-	-
Endometritis	06(3.3%)	-	06(2.97%)	-	-	-
Polyp	04(2.2%)	-	03(1.5%)	-	-	-
Atrophic	08 (4.4%)	07(2.5%)	04(1.98%)	20(8%)	-	-
Endoca	02(1.1%)	-	04(1.98%)	-	-	-
Pregnancy	06(3.3%)	-	01(0.51%)	-	Others 2(1.06%)	Others 38(25.3%)
Inadequate	11(6.0%)	16(5.62%)	06(2.97%)	-	-	06 (4.0%)

Discussion

The endometrium is undergoing regular cyclical changes in response to the recurrent hormonal changes of the ovulatory cycles thus it is crucial to take endometrial sample at an appropriate time of ovulatory cycle. Inadequate clinical information also leads to erroneous diagnosis. AUB with organic cause can be due to reproductive disease, iatrogenic causes and systemic diseases. When no specific cause of AUB is found, then by exclusion, a diagnosis of dysfunctional uterine bleeding (DUB) is assumed.

AUB occurs as heavy, prolonged or acyclic flow at perimenopausal period or as spotting or minimal bleeding at post-menopausal period and requires proper evaluation to rule out malignancy. In the current study 183 specimens of endometrium (curettage/biopsy) were evaluated in order to find age, clinical and pathological

features. The incidence of abnormal uterine bleeding was more in perimenopausal age group than postmenopausal age group. This might be due to earlier evaluation. In our study majority of patients belonged to 41-50 years age group. This is in concordance to the studies done by Sarika et al [5], Doraiswami S et al [6] and Muzaffar et al [7]. whereas the study conducted by Rajesh Patil et al [8] and Mitra K et al [9] showed AUB predominantly in a decade earlier i.e. age group 31-40 year and was recorded to be 45.2% and 62% respectively.

The most common bleeding pattern encountered in present study was heavy menstrual bleeding 57.3% which is comparable with the study by Ayesha Fatima [10] and Rajesh Patil et al [8]. Comparison of various histopathological patterns of endometrium in AUB by

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various authors is shown in Table 6. Normal physiological phases of endometrium, such as proliferative and secretory pattern were encountered in maximum number of cases. Proliferative endometrium comprised of 71 cases (38.8%) in our study, this finding is in very much alliance with the studies done by Sarika et al [5], Rajshri P et al [11] and Khare et al [12]. This is followed by secretory endometrium in 30(16.3%) cases.

The third commonest lesion was hyperplasia observed in 22 (12%) cases with its maximum number of patients falling in the age group of 41 to 50 years which is comparable with study done by Sarika et al [5] (15.3%) and is in discordance with the studies done by Rajesh Patil et al [8] (40%), Anuradha salviet al [13] (25.2%), Bhoomika Dadhanania et al [14] (26.7%), who observed a high incidence of endometrial hyperplasia. Endometrial hyperplasia is commonly seen in perimenopausal age group due to failure of ovulation. Persistent unripe follicles expose the endometrium to excessive and prolonged estrogenic action. The incidence of simple hyperplasia was more common in the perimenopausal age group. In our study there were only two cases (9%) of complex hyperplasia with atypia, this is in contrast to the findings of Rajshri P et al [11], Khare et al [12] who observed a higher incidence of 19.35% & 33.3% respectively.

12(6.5%) cases showed disordered proliferative pattern in our study, which is in accordance with Jetley S et al [15]. The term 'disordered proliferative endometrium' is a complex term that denotes an endometrium that is hyperplastic but without an increase in endometrial volume. Although it resembles a simple hyperplasia, but the process is focal rather than diffuse. Hormonal change on endometrium was seen in 11(6.0%) cases in our study which was in concordance with the study done by Sarkiaet al [5] who reported 13 cases (6.43%). But Khare et al [12] showed effects of hormones in 9 cases only, whereas Abidet al [16] showed a higher incidence of 27%.

Patients with chronic endometritis can present with AUB, pelvic pain and infertility, which are distressful symptoms and thus needs to be timely and accurately diagnosed because with specific treatment endometrium starts functioning normally. Study done by Jetly et al [15] found 20 cases of endometritis which is quite a higher incidence comparing to our study in which this condition was diagnosed in few patients (6 cases), out of which 3 cases shows acute on chronic endometritis, 2 cases showed chronic endometritis and remaining 1 case showed necrotizing granulomatous endometritis

with cystic change. Atrophic endometrium was seen between 41-60 years age group i.e. premenopausal and postmenopausal age groups. The incidence of atrophic endometrium in the present study (4.4%) is lower as compared with results shown by Abdullah LS et al [17] and Sarika et al [5]. It is now well known that atrophic endometrium leads to bleeding and it is postulated to be due to anatomical changes in the vasculature or abnormalities in the local haemostatic mechanisms. The expanding cystic glands lead to distension and thinning of veins overlying these glands and eventually making the vessel prone to injury.

Endometrial polyps are defined as polypoidal fragments lined with epithelium on its three sides, fibrous stroma and thick walled blood vessels. The incidence of endometrial polyp was (2.2%) in our study, which is in accordance with Jetley S et al [15] (2.7%) and Doraiswami S et al [6] in (11.2%). 2 cases (1.1%) of endometrial carcinoma were found in this study which is common in post-menopausal age group. This finding is comparable to the findings in Sarikaet al [5] (1.98%).

On the contrary, this finding is lower than the incidence recorded by Doraiswami et al [6] (4.4%), Khare et al [12] (3.7%) & Bhatta et al [18] (5.7%). Endogenous and exogenous hyperestrogenism is the most common risk factors for endometrial carcinoma. The most common precursor lesion for endometrial carcinoma is endometrial hyperplasia. Changes of pregnancy were seen in 6(3.3%) cases in 15-40 year age with findings of RPOC, partial mole, complete mole and Arias-stella reaction. Eleven cases (6.0%) of endometrial biopsies were scanty and inadequate for opinion.

Conclusion

The histopathological study of endometrium in females with abnormal uterine bleeding in all the age groups plays an important role in diagnosing various histopathological patterns and aetiopathological factors.

Present study confronted a wide spectrum of histomorphological changes in endometrial biopsies of patients presenting with AUB ranging from normal endometrium to malignancy.

However histopathological evaluation of endometrial biopsies is a challenging task for pathologist due to the frequent inadequate endometrial sampling requiring proper screening of endometrial samples for prompt but accurate diagnosis.

Findings: Nil; **Conflict of Interest:**

Non initiated. **Permission from IRB:** Ye

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