

## Endometrial histopathology in abnormal uterine bleeding

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### Abstract

**Introduction:** In routine practice abnormal uterine bleeding (AUB) is a distinct entity. In women of reproductive age with episodic unpredictable bleeding it is an indication of number of pathologic disorder. Histopathological assessment of endometrial curetting's has high sensitivity.

The present study was done in suspected AUB patients to evaluate histopathological patterns in endometrial biopsy among different age groups.

**Methodology:** A retrospective study done on 284 cases at tertiary teaching hospital, Karnataka. The study period was from Jan 2015 to April 2016. Clinical history and findings were collected and recorded. The histopathology study of endometrial patterns and age specific correlation was made.

**Results:** The majority of cases belonged to the age group of (41-50) years. The frequent histopathologic pattern was proliferative and secretory in (41.54% and 13.38% respectively). Endometrial hyperplasia in (34.50%) cases in fourth and fifth decades was the commonest pathology. Among these atypical hyperplasia constituted for ( 6.12%) cases. Endometrial carcinoma was diagnosed in (1.40%) cases in the post-menopausal age group .Chronic non-specific endometritis was noted in (2.11%) cases.

**Conclusion:** AUB has been reported to cause a significant impact on quality of women' s health ranging from infertility to premalignant and malignant changes in the endometrium. So evaluation of endometrial curettings would help to assess the functional status of endometrium for an effective planned treatment.

**Keywords:** Endometrium, Abnormal uterine bleeding, Menorrhagia, Histopathology.

### Introduction

Menstrual disorders continues to be a challenging disorder among women of all age groups.<sup>(1)</sup> Abnormal uterine bleeding (AUB) is considered as irregular, unpredictable uterine bleeding that occurs in the absence of recognizable pelvic pathology, general medical diseases or during pregnancy.<sup>(2)</sup> The normal menstrual cycle is between 24 days and 38 days lasting up to 8 days.<sup>(3)</sup> In relation AUB is defined as bleeding from uterine corpus that is abnormal in volume, regularity and / or timing and that has been present for majority of the past 6 months.<sup>(4)</sup> In India a prevalence of 17.9% is reported.<sup>(3)</sup> It is reported to occur in 9-14% among women between menarche and menopause.<sup>(5)</sup>

AUB in 90% of cases are anovulatory and 10% ovulatory.<sup>(6)</sup> Anovulatory bleeding is common in adolescents( 20%) and in Perimenopausal women ( 50%).<sup>(2)</sup> Anovulatory cycles cause estrogen break through or estrogen withdrawal bleeding.<sup>(2)</sup> Ovulatory bleeding represent a possible endocrine dysfunction with progesterone withdrawal bleeding.<sup>(6)</sup> So in AUB cyclic endometrial stimulation is lost that arises from the ovulatory cycle.<sup>(2)</sup>

AUB is a diagnosis of exclusion.<sup>(6)</sup> The causes includes organic and non-organic. The organic may be grouped into reproductive tract and systemic diseases with iatrogenic causes.<sup>(1)</sup> Reported in more than 70% in peri and post- menopausal women.<sup>(7)</sup> In premenopausal period pregnancy, endometritis, cervicitis and cancer cervix with clotting factor disorders, hypothyroidism,

liver and chronic renal diseases is to be considered.<sup>(8)</sup> During menopause endometrial causes includes hyperplasia, atrophy, cancer, polyps, fibroids and endometritis. In adolescents coagulation disorders should be excluded.<sup>(6)</sup> Coagulopathies would affect 13% of women with heavy bleeding.<sup>(9)</sup>

Heavy menstrual bleeding (HMB) is the commonest complaint. It affects 14-25% women of reproductive age.<sup>(9)</sup> Over 5% of patients in the age group (30-49) years consulted gynaecologist each year with this complaint.<sup>(10)</sup> The terminologies menorrhagia, metrorrhagia, menometrorrhagia and dysfunctional uterine bleeding are poorly defined and confusing.<sup>(11)</sup> So a new classification system for the umbrella diagnosis of AUB would define as abnormal uterine bleeding with heavy menstrual bleeding (AUB/HMB) and Abnormal uterine bleeding with bleeding between periods (AUB/IMB).<sup>(11)</sup> The International Federation of Gynecology and Obstetrics (FIGO) Menstrual disorders Working Group proposes to abandon the terminology dysfunctional uterine bleeding (DUB), while advocate to use the terms AUB and heavy menstrual bleeding.<sup>(3)</sup> In 2011 FIGO<sup>(12)</sup> the causes of AUB have been categorized into nine categories and represented as acronym (PALM- COEIN). PALM includes; Polyps (AUB-P), adenomyosis (AUB-A), leiomyoma (AUB-L) and malignancy and hyperplasia (AUB-M). The group COEIN included; coagulopathy (AUB-C), Ovulatory dysfunction (AUB-O), endometrial (AUB-E), iatrogenic (AUB-I) and not yet specified (AUB-N).<sup>(11,9)</sup>

HMB is introduced as part of the( PALM-COEIN) classification system.<sup>(13)</sup>

Thus the significance of AUB relates to its major impact on women's quality of life in the reproductive age, productivity and utilization of health care services.<sup>(1,4)</sup> Improperly managed anovulatory bleeding would cause endometrial hyperplasia and endometrial carcinoma.<sup>(2)</sup> There is an increased risk for iron deficiency anaemia and cardio vascular morbidity. Anovulation is associated with infertility.<sup>(2)</sup> AUB affects 30% of women during reproductive years.<sup>(14)</sup> In spite of detailed clinical assessment the cause of the bleeding could be established in only 50-60% of the AUB cases.<sup>(15)</sup> Clinico pathologic correlation of endometrial biopsy samples could remain a diagnostic standard for the effective diagnosis of endometrial pathology and its management.<sup>(1)</sup>

### Methodology

A descriptive study conducted in the department of pathology of a Government teaching hospital, from January 2015 to April 2016 after obtaining permission from Institutional Ethical Committee. Total of 284

cases of endometrial pathology as cause of AUB was studied. Cases of leiomyoma, adenomyosis, polyps, cervical and vaginal pathology, pelvic inflammatory diseases and coagulation disorders were excluded from the study. Samples obtained through D & C were routinely formalin fixed and processed. The 5-micron thick sections were stained with haematoxylin and eosin and examined for histopathological changes. The age specific correlation for individual cases was analyzed. The clinical details and investigation reports of the cases were obtained from individual case requisitions submitted to the department of pathology and medical records department. The data was collected and tabulated in Microsoft excel sheet. The percentages were calculated for purpose of comparison.

### Results

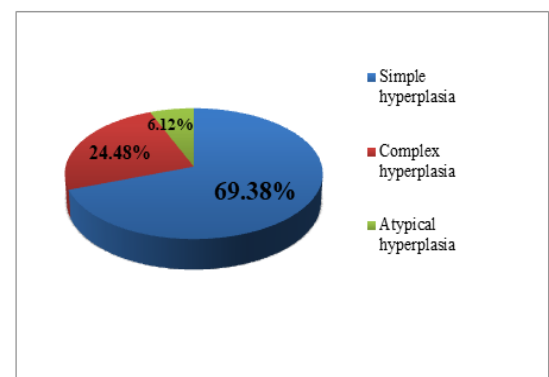
The study patients were divided into six groups (Table 2). The commonest age group affected was 41-50 (38.73%) years. This was followed by more frequent cases in the 31-40 (33%) age group. Minimum cases was seen in <20 years age group (3.87%).

**Table 2: Distribution of AUB in different age groups**

	Group 1 < 20yrs	Group 2 21-30yrs	Group 3 31-40yrs	Group 4 41-50yrs	Group 5 51-60yrs	Total
Proliferative Endometrium	8	18	39	48	5	118
Secretory Endometrium	2	14	18	4	-	38
Chronic endometritis	-	3	2	1	-	06
Atrophic endometrium	-	-	1	5	3	09
Disordered proliferative endometrium	-	1	5	2	3	11
Endometrial hyperplasia	1	11	29	48	9	98
Endometrial carcinoma	-	-	-	2	2	4
<b>TOTAL</b>	<b>11 (3.87%)</b>	<b>47 (16.5%)</b>	<b>94 (33%)</b>	<b>110 (38.73%)</b>	<b>22 (7.74%)</b>	<b>284</b>

Histopathology showed various patterns of endometrial changes (Table 1). The physiological phases of proliferative pattern in 118 (41.54%) and the secretory pattern in 38 (13.38%) cases respectively was noted. Disordered proliferative pattern was observed in 4(1.40) cases. In the study hyperplasia was the most common pathology in 98 (34.50%) cases in 41-50 year age group. (Graph 1) depicts simple hyperplasias in 68(69.38%), complex hyperplasias in 24 (24.48%) and complex hyperplasias with atypia in 6(6.12%) cases respectively. Endometrial adenocarcinoma was diagnosed in 4 (1.40) cases who presented with post-menopausal bleeding in fifth and fourth decades. So age specific comparative analysis showed high incidence of endometrial hyperplasia and carcinoma in perimenopausal and postmenopausal women. Atrophic endometrium was observed in 5.63% cases in > 45 years age. Chronic endometritis was common in the active reproductive age group accounting for 2.11% cases.

It was noted that the majority of patients presented with complaint of menorrhagia. Others presented with polymenorrhagia, perimenopausal and post-menopausal continuous bleeding.



**Graph 1: Distribution of subtypes of endometrial hyperplasia**

**Table 1: Distribution of histopathologic patterns of endometrium**

	No. of cases (n=284)	Percentage (%)
Proliferative phase endometrium	118	41.54
Secretory phase endometrium	38	13.38
Chronic endometritis	06	2.11
Atrophic endometrium	09	3.2
Disordered proliferative endometrium	11	3.87
Endometrial hyperplasia	98	34.50
Endometrial carcinoma	4	1.40

## Discussion

Abnormal uterine bleeding is a regular complaint in gynecologic practice. It is reported that the most likely aetiology may coincide to perimenopausal, premenopausal and postmenopausal age group<sup>(1,4)</sup> A 96% sensitivity for detection of histopathologic abnormalities in samples of endometrial biopsy is reported.<sup>(1,4)</sup>

In the present study of 284 AUB cases it was observed that the frequency of menstrual irregularity increased in the advancing age group. The maximum cases observed were in the age groups 41-51 (38.73%) and 31-40 (33%). Singh A. and co-author studied 300 similar cases and noted maximum cases in the comparable age group in 41-50 (48.6%) and in 31-40 (36.3%).<sup>(4)</sup> Doraiswami S. and authors study on 409 cases also reported a significant occurrence of menstrual disorders with advancing age.<sup>(1)</sup> This finding could be due to the anovulatory cycles occurring in their climacteric period of menopause where in the number of ovarian follicles decline and the estradiol level fall leading to shorten cycles which often become intermittently anovulatory.<sup>(1)</sup>

In the adolescent age group <20 years accounted for (3.87%) cases with normal pattern of proliferative and secretory endometrium. A case of simple hyperplasia in a 18 year patient was noted. Doraiswami S. and co-authors observed a similar finding accounting for 1.5% cases<sup>1</sup>. It has been reported that the prevalence of a primary coagulation disorder in this age group requiring emergency treatment ranged from 3 to 20%<sup>(1)</sup> and hence should be evaluated for coagulopathy.<sup>(1,6)</sup>

The commonest pattern of bleeding abnormality noted in our patients was menorrhagia and polymenorrhagia. In an observational study on 1362 cases by Kotagasti T reported that menorrhagia was highest presenting complaint accounting for (33%) cases.<sup>(10)</sup> The same observation was noted in other similar studies.<sup>(1,4)</sup>

The commonest endometrial pattern studied in our patients was of proliferative pattern in 118 (41.54%) cases, a finding comparable in the study by Singh A and co-author with (37%) cases.<sup>(4)</sup> Secretory pattern was noted in 38 (13.38%) among our cases. Authors Gopalan and others in their study on 905 cases have

reported a near comparable incidence (16.1%).<sup>(16)</sup> But a comparatively high incidence of (30%) was noted by Singh A and co-author<sup>(4)</sup>

Disordered proliferative pattern in our patients was seen in 11 (3.87%) cases with maximum cases in 31-40 age groups, Singh. A and co-author in their observation found an incidence of ( 5.6%) and maximum in 41-50 age group .<sup>(4)</sup> Doraiswami S and co-authors noted this pattern of endometrium in a significant number of 84 cases commonly in the 31-40 years and 41-50 years age groups respectively.<sup>(1)</sup> This pattern would not seem appropriate for any time in the normal menstrual cycle; but abnormal enough to be considered hyperplastic and without an increase in endometrial volume.<sup>(17)</sup> On histopathology examination this would resemble a simple hyperplasia which is seen as a focal change rather than a diffuse process<sup>1</sup>. So in the spectrum of proliferative lesions disordered proliferative pattern would lie at one end and carcinoma at the other end with intervening stages of hyperplasia. So early diagnosis and timely treatment would prevent the disease progression.<sup>(1)</sup>

We noted Atrophic endometrium in the age group 41-50 years accounting for (5.63%) cases. Doraiswami S. and authors found these cases often in fifth and sixth decade age groups.<sup>(1)</sup> Singh A. and co-author report an incidence of (3%) commonly in > 40 years women.<sup>(4)</sup> The underlying mechanism of bleeding in this age group could be due to anatomical vascular variation which would risk the thin walled veins vulnerable to injury that are present superficial to the expanding cystic glands.<sup>(1)</sup> Also an abnormal local hemostatic mechanism in the uterus could become contributory.<sup>(1,4)</sup>

The commonest pathology diagnosed in our study was endometrial hyperplasia in a total of 98 (34.50%) cases. The Subtypes included maximum cases of simple hyperplasia in (69.38%) followed by complex hyperplasia of (24.48%) and complex hyperplasia with atypia in (6.12%) cases (Graph1) in 41-50 years group patients. Authors Singh A and Ramana Bai PV in their study had diagnosed endometrial hyperplasia in (22.2%) cases and common in >40 years patients.<sup>(4)</sup> Authors Muzaffar M and others studied 260 cases and reported endometrial hyperplasia in ( 24.7%.) cases.<sup>(18)</sup> In another similar study Taludkar B. and co-authors reported hyperplastic endometrium in (56.31%) cases.<sup>(7)</sup> Endometrial hyperplasias are recognised to be the precursors of endometrial carcinoma. The association of underlying risk factors like obesity, diabetes, increased intake of animal fat and sedentary life style is to be noted.<sup>(1)</sup>

We noted endometrial adenocarcinoma (1.40%) cases with equal numbers in the age group of 41-50 years and 51-60 years age group. Singh A and co-author observed an incidence of (1%) among 300 cases and in more than 50 years age group.<sup>(4)</sup> Doraiswami S. and authors study on 409 patients the incidence of carcinoma were more common in the 51-60 years age

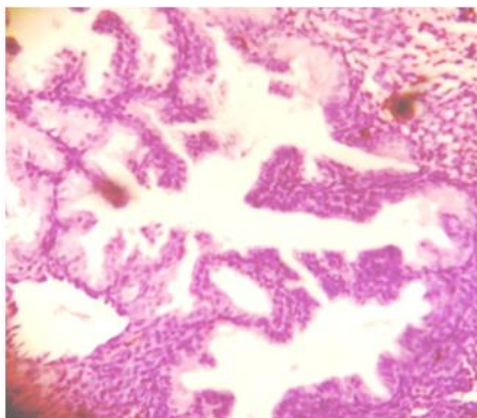
group.<sup>(1)</sup> Thus the age specific incidence of endometrial hyperplasia and carcinoma in perimenopausal and postmenopausal women were comparable. Dangal G and authors in their study on 84 AUB cases documented a lower incidence of endometrial cancer which could be attributed to the practice of early child bearing and multiparity.<sup>(19)</sup>

Chronic non-specific endometritis was present in (2.1%) of our cases in less than 40 years age group. An incidence of (1.6%) with most cases in 31-40 years age group were observed by Singh A. and co-author<sup>4</sup>. These patients would also present with pelvic pain and infertility. With diagnosis and specific treatment endometrium would start functioning normally.<sup>(1)</sup>

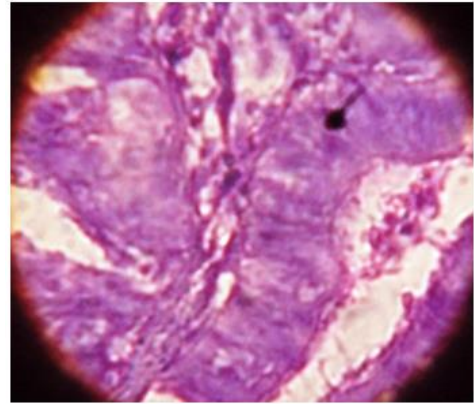
Table 3: Depicts the comparison of predominant histopathological pattern of endometrium and maximum age distribution of AUB cases among various studies.

**Table 3: Comparison of histopathologic pattern and age group among various studies**

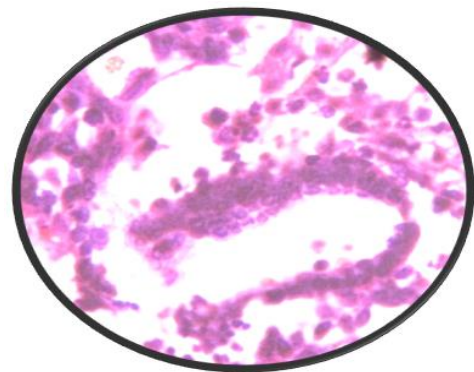
Sl. No.	Study ( Year)	Maximum Age Group (in years)	Predominant Pathological pattern of endometrium studied
01.	Doraiswami S et al. (2011) <sup>1</sup>	41-50	Disordered proliferative endometrium
02.	Malukani P et al. (2013) <sup>20</sup>	31-40 (48%)	Hyperplasia
03.	Parmar et al. (2013) <sup>21</sup>	30-40	Disordered proliferative endometrium (33.33%)
04.	Gopalan U et al. (Jan 2015-Dec 2016) <sup>16</sup>	40-49	Endometrial hyperplasia (56.31%)
05.	Singh A et al. (Jan 2016) <sup>4</sup>	41-50 (48.6%)	Endometrial hyperplasia ( 22.6%)
06.	Muzaffar M. et al.(2005) <sup>18</sup>	41-50	Endometrial hyperplasia (24.7%)
07.	Taludkar B et al. (2016) <sup>7</sup>	40-45	Hyperplastic endometrium
08.	Present study (2015-16)	41-50	Endometrial hyperplasia; (34.58%)



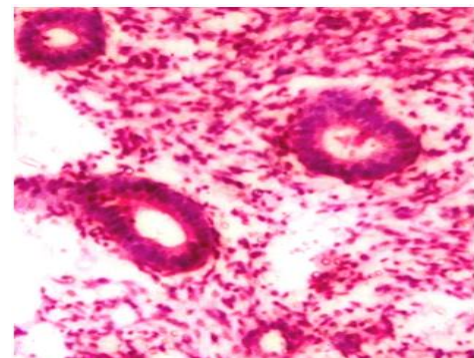
**Fig. 1: Microphotograph showing complex endometrial hyperplasia without atypia (H & E, 10x)**



**Fig. 2: Microphotograph showing complex hyperplasia with atypia (H & E, 40x)**



**Fig. 3: Microphotograph showing adenocarcinoma endometrium (H & E, 40x)**



**Fig. 4: Microphotograph of Chronic endometritis showing inflammatory infiltrate surrounding endometrial glands (H & E, 10x)**

**Conclusion**

AUB affects 1 in 5 women at some point during their reproductive life span.<sup>(22)</sup> Histopathological reporting of endometrial curetting has proved to be an effective and safe evaluation tool to make a specific diagnosis.<sup>(1)</sup> In the present study a age specific wide spectrum of endometrial changes was observed. A structured approach to establishing the cause using the FIGO PALM-COEIN classification system could facilitate an accurate diagnosis and management options.

### Acknowledgement

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Conflict of interest: None declared.

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