



ENDOMETRIAL LESIONS' HISTOPATHOLOGICAL PATTERNS IN WOMEN WITH ABNORMAL UTERINE BLEEDING

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ABSTRACT

BACKGROUND: Unusual bleeding from the uterus (AUB) is one of the most frequent and difficult issues that gynecologists encounter. The best diagnostic method for assessing AUB is the histopathological analysis of an endometrial sample. The most frequent presenting symptom in the gynecology outpatient department is abnormal uterine bleeding (AUB). While endometrial sampling may be useful as the initial diagnostic step in AUB, pathologists in practice may occasionally find it difficult to interpret the results. In order to determine the endometrial etiology of AUB, this study examined the endometrium's histology. Additionally, we made an effort to track the prevalence of different pathologies in age groups that presented with abnormal uterine bleeding.

AIM: The aim of the study was to determine the spectrum of endometrial pathologies in different age groups of patients presenting with AUB.

MATERIAL AND METHOD: The Department of Pathology carried out this retrospective investigation. By using inclusion and exclusion criteria, 100 cases in total were analyzed. The following patients were excluded: those having a gestational cause, hemostatic conditions, isolated cervical or vaginal disease, and leiomyoma. The case records from the Medical Records Department were used to gather pertinent clinical information regarding age, pattern, and duration of abnormal bleeding, menstrual history, obstetric history, use of exogenous hormones, physical and gynecological examination findings, lab investigation results, and sonological and hysteroscopic findings. A very well-structured proforma was used to record all the data. Hysterectomy or endometrial curetting were used to extract endometrial specimens, which were then fixed in 10% formalin.

RESULTS: The age of patients ranged from 23-60 years. The mean age of women presented with AUB in our study was 40.2 years. The maximum number of patients 70 were in the age group 41-50 years, followed by 60 patients in the age group of 31-40 years. Out of 150 patients, 90 were due to functional causes as no organic pathology was found, while 60 cases showed definite endometrial pathology. Out of 90 functional causes of AUB, proliferative endometrium 49 was the most common pattern. Out of 60 organic causes, endometrial hyperplasia 40 was the most common. Out of the 40 cases of endometrial hyperplasia, 22 cases of simple hyperplasia without atypia, 2 cases of simple hyperplasia with atypia, 8 cases of complex hyperplasia without atypia, and a single case of complex hyperplasia with atypia.

CONCLUSION: AUB is brought on by age-related disease in the endometrium. AUB is evaluated using endometrial biopsy histopathology as a key diagnostic technique, and a definite diagnosis could aid the doctor in formulating a treatment strategy for the effective management of AUB. Endometrial biopsy and curettage histopathological patterns in women with AUB are varied. These lesions range from straightforward physiological to incredibly complex pathological ones. The vast majority of the lesions causing AUB found in this investigation were fetal lesions, which are most frequently found in female reproductive patients.

KEYWORDS: Abnormal Uterine Bleeding (AUB); Dysfunctional Uterine Bleeding (DUB), Endometrial Lesions and Histopathological Pattern

INTRODUCTION

AUB is characterized as a bleeding pattern that is different from patterns seen during a typical menstrual cycle or after menopause in terms of frequency, length, and amount.¹ It is regarded as one of the most prevalent and difficult issues that gynecologists encounter. About one-third of all outpatients who visit the gynecological OPD do so because of it.^{2,3} Heavy bleeding can lead to issues like iron deficiency in affluent countries and chronic sickness in developing countries, which can have an impact on a woman's health both physically and socially.⁴ One of the most prevalent gynecological conditions that affect women worldwide is endometrial disease.⁵ All age groups are affected by these illnesses, which also considerably raise maternal morbidity and mortality rates. AUB is the primary presenting symptom in the majority of female patients with endometrial disorders.^{5,6} AUB thus supports the requirement for an urgent diagnosis. This is due to the broad variety of endometrial disorders' histological patterns. These lesions range from straightforward conditions like endometrial hyperplasia to more serious conditions like endometrial cancer.⁶ The two most crucial sample techniques for determining the precise diagnosis of the lesions are endometrial biopsy and curettage.⁷ AUB's etiology changes with age, thus the first step is to rule out pregnancy-related factors based on the patient's medical history and the presence of the human chorionic gonadotropin b-subunit.⁸ After excluding pregnancy, a thorough investigation using the PALM-COEIN classification proposed by The International Federation of Gynecology and Obstetrics (FIGO) focuses on causes by structural pathologies (Polyps, Adenomyosis, Leiomyomas, and Malignancy or atypical endometrial hyperplasia [PALM]) while the "COEIN" causes are non-structural and are diagnosed by a wider approach of clinical assessment, history, and sometimes laboratory tests (Coagulopathies, Ovulatory disorders, primary Endometrial disorders, Iatrogenic and Not otherwise classified; COEIN).⁹ By examining the histological changes of the endometrium and taking into account the woman's age, the stage of her menstrual cycle, and the usage of any exogenous hormones, the underlying disease can be identified. Younger patients are more likely to experience pregnancy-related and dysfunctional

uterine hemorrhage, whereas elderly patients are more likely to develop atrophy and organic lesions. Fewer than 10% of postmenopausal patients undergoing biopsy have endometrial cancer, while up to 16% of them have hyperplasia.¹⁰ Patients who have used exogenous estrogen, have a history of anovulation, are more likely to develop hyperplasia and cancer.¹⁰ To determine the precise nature of the lesion and rule out cancer in perimenopausal and postmenopausal women, early assessment is crucial. Most young women of reproductive age exhibit changes linked to hormone imbalance more frequently.¹¹ However, endometrial hyperplasia and endometrial cancer are more prevalent in older women in the premenopausal and postmenopausal age groups.^{12,13} According to reports, endometrial cancer ranks first among gynecological malignancies in industrialized nations and second among those in developing nations, after cervical cancer.¹² Endometrial cancer, which makes up 6% of all gynecological cancers and is the third most common cause of death from gynecological malignancy after ovarian and cervical cancers, is confirmed by studies conducted in the United States.¹⁴ In most instances DUB is due to the occurrence of an anovulatory cycle.¹⁵ It can be identified using a variety of diagnostic approaches when structural, iatrogenic, pharmaceutical, psychiatric, and systemic problems have been ruled out. The gold standard diagnostic method for assessing AUB is histopathological examination of endometrial biopsies. A precise diagnosis aids in the planning of the therapy for effective, resourceful management of AUB, when hysterectomy is not the solution but rather the interaction of hormones.¹⁶

MATERIAL AND METHODS

The Department of Pathology carried out this retrospective investigation. By using inclusion and exclusion criteria, 100 cases in total were analyzed. The following patients were excluded: those having a gestational cause, hemostatic conditions, isolated cervical or vaginal disease, and leiomyoma. The case records from the Medical Records Department were used to gather pertinent clinical information regarding age, pattern, and duration of abnormal bleeding, menstrual history, obstetric history, use of exogenous hormones, physical and gynecological examination findings, lab investigation results, and sonological and

hysteroscopic findings. An very well-structured proforma was used to record all the data. Hysterectomy or endometrial curetting were used to extract endometrial specimens, which were then fixed in 10% formalin. The samples underwent standard processing and were stained with the H&E stain. Functional and organic factors were distinguished between when classifying the histopathological findings of AUB. Age, clinical history, a digital rectal examination, and a clinical diagnosis were all recorded.

Inclusion criteria:

➤ Women presented with AUB in all age groups.

Exclusion criteria:

The study excluded patients with hemostatic diseases, cervical pathology, pregnancy-related problems, and bleeding from leiomyomas.

Specimen sampling and laboratory procedure

Dilation and evacuation (D&E) or D&C under hysteroscopy were both used to perform biopsies in inpatient settings. In a D&C, the cervix is dilated after the sound is passed in order to determine the size and orientation of the uterus. The cervix is already dilated during D&E. Once the uterus has sufficiently dilated, the anterior, posterior, two lateral, and fundus of the uterus are all curetted before the material is collected in a container containing 10% formalin and delivered to the pathology lab for analysis. The endometrial tissues were then fixed in 10% formalin to create pathology slides. Hematoxylin and eosin stain was applied after the paraffin-embedded tissues had been cut into sections. Pathologists examined sections under a light microscope. The LIECA automatic tissue processor processed the tissue fragments, and paraffin blocks were created. Hematoxylin and eosin (H&E) stain was applied to

tissue sections (4-6 μ). To minimize observer bias, two pathologists each performed a separate microscopic examination. The typical cycle endometrium (proliferative and secretory phases) and other aberrant changes in the endometrium, such as atrophic endometrium, disordered proliferative endometrium, insufficient secretory phase, and irregular shedding, were included in this study as functional reasons of AUB. In this study, organic intrauterine lesions such as chronic endometritis, endometrial hyperplasia, benign endometrial polyps, endometrial cancer, and endometrial stromal nodules were the causes of AUB. The results of a thorough histological investigation were recorded. Medical records were consulted for demographic information, parity, gestational age if pregnant, the indication, and histopathological findings. Patients were divided into groups based on their ages and parity status.

STATISTICAL ANALYSIS

Descriptive statistics such as mean, SD, and percentage were used. Statistical analysis between age and specific endometrial causes was done using a chi-square test and p-value <0.05 were considered statistically significant. Analysis was done in the form of percentages and proportions and represented as tables and figures where necessary.

RESULT: -

The age of patients ranged from 23-60 years. The mean age of women presented with AUB in our study was 40.2 years. The maximum number of patients 70 (46.67%) were in the age group 41-50 years, followed by 60 patients (40%) in the age group of 31-40 years. The distribution of cases according to the age group is shown in Table 1.

Table 1: Distribution of cases according to age group

Age group(Years)	No. of patients	Percentage
21-30	6	4
31-40	60	40
41-50	70	46.67
>50	14	9.33
Total	150	100

Table 2: Distribution of cases of AUB according to cause

Cause of AUB	No. of patients(n=150)	Percentage
Functional Cause	90	66.67%
Organic cause	60	33.33%

A total of 150 patients presented with AUB were analyzed. Out of 150 patients, 90 (66.67%) were due to functional causes as no organic pathology was found, while 60 (33.33%) cases showed definite endometrial pathology. Out of 90 functional causes of AUB, proliferative endometrium 49 (54.4%) was the most common pattern. Out of 60 organic causes, endometrial hyperplasia 40(66.67%) was the most common.

Table 3: Distribution of cases of AUB according to histological pattern

Histological diagnosis	Total no.of cases (n=150)	Percentage
Proliferative phase	36	24
Secretory phase	10	6.67
Atrophic	20	13.3
Disordered proliferative endometrium	19	12.66
Deficient secretory phase	5	3.3
Chronic Endometritis	5	3.3
Endometrial polyp	16	10.67
Simple hyperplasia without atypia	22	14.67
Simple hyperplasia with atypia	3	2
Complex hyperplasia without atypia	7	4.67
Complex hyperplasia with atypia	1	0.67
Endometrial carcinoma	4	2.67
Endometrial stromal nodule	1	0.67
Irregular shedding	1	0.67
Total	212	100

Histopathological examination revealed various patterns in AUB as illustrated. Normal cyclical pattern: proliferative and secretory phases were the most common and seen in 60 (40%) patients. Endometrial hyperplasia and disordered proliferative endometrium were the next common histological patterns seen in 40 (26.67%) and 20 (13.33%) cases, respectively. Out of the 40 cases of endometrial hyperplasia, 22 cases of simple hyperplasia without atypia, 2 cases of simple hyperplasia with atypia, 8 cases of complex hyperplasia without atypia, and a single case of complex hyperplasia with atypia. Atrophic endometrium was seen in 20 (13.3%) cases, endometrial polyp in 16 (10.67%) cases, and endometrial carcinoma in 4 (2.67%) cases. Out of 4 cases of endometrial carcinoma, 3 cases were well-differentiated endometroid adenocarcinoma and one was moderately differentiated endometroid adenocarcinoma. One of the cases was of well-differentiated endometroid adenocarcinoma showing squamous metaplasia. In our study, only one case of the endometrial stromal nodule (0.67%) was found.

DISCUSSION

The endometrium is a reflection of a woman's hormonal state. Endometrium exhibits histological variance depending on the age of the woman, the menstrual cycle stage, and any further unique pathology.¹⁰ In typical cycles, endometrial growth stimulated by estrogen follows menstrual shedding. The endometrial glands expand and enlarge during this stage.¹⁷ On the ninth postovulatory day, spiral arterioles are formed as a result of endothelial proliferation, wall thickening, and coiling throughout the second part of the menstrual cycle.^{17,18} The most frequent and puzzling issue affecting women of all ages is AUB. Any bleeding that does not meet the requirements of typical menstrual bleeding has been referred to as abnormal uterine bleeding. Numerous illnesses of the reproductive system and non-gynecological factors are among the causes of irregular uterine bleeding. Iatrogenic causes, systemic diseases, and diseases of the reproductive tract are three categories of organic causes of irregular uterine bleeding. Dysfunctional uterine bleeding (DUB) is the most likely diagnosis when an organic cause of AUB cannot be identified. A clearly characterized

organic anomaly is the cause of abnormal uterine bleeding in roughly 25% of individuals.¹⁹ Pregnancy complications were frequent among women between the ages of 21 and 30. Since most women conceive at this age, this can be explained. Until shown differently, pregnancy should be thought of as a complication of pregnancy. Patients in this age group who appear with abnormal uterine bleeding should be looked into and tested for pregnancy using a urine gravidity index.²⁰ In this investigation, a sizable portion of the cases displayed disorganized proliferative patterns. The spectrum of proliferative lesions of the endometrium comprises cancer at one end and disorganized proliferative patterns at the other, with phases of hyperplasia in between. "Disordered proliferative endometrium" has been used in a variety of contexts and is a little challenging to define. It indicates a hyperplastic endometrial appearance without an increase in endometrial volume.²¹ appears normal at any one point in the menstrual cycle, but is not aberrant enough to be categorized as hyperplastic. Simple hyperplasia is similar to the disorganized proliferative pattern, but the process is focused rather than diffuse. A higher incidence of the disordered proliferative pattern was found in our study as compared to **Cho Nam-Hoon et al.1989**²² Prolonged estrogen stimulation also results in the formation of the endometrial polyp.²³ The incidence of benign endometrial polyps was 8% in this study which was similar to **Silander 1962**²⁴ 6.66%. The higher incidence was found in **Parmar J et al2013**¹⁶ 10.78% & **Doraswami S. et al2011**²⁵ 11.2%. In our study, a higher incidence of 47.1% was seen in the 41–50 years age group; similar to another study.²⁶ A potential spontaneous regression mechanism, which is a feature of the cycling endometrium in the reproductive age group, could be the cause of the lower incidence of endometrial polyps in the younger age group.²⁵ A study done by **Dangal et al.2003**²⁷ in Nepal documented a lower incidence of endometrial cancer in Nepalese women attributing it to the practice of early childbearing and multiparity. Possibly, the same factors contributed to a lower incidence of carcinoma in our patients. Chronic endometritis, diagnosed in 2.4% of cases concurs with the reported incidence of 2.6% by **Rupal shah et al2014**²³ Majority of them were > 40 years of age group similar to the study by **Damale**

et al 2013²⁸. Chronic endometritis, characterized by irregular fibrotic stroma & infiltration of lymphoplasmacytic cells has been known to follow pregnancy or abortion & may be the result of IUCD or accompanied by mucopurulent cervicitis & PID.²⁹

AUB is evaluated using endometrial biopsies' histopathological testing, which reveals a variety of patterns ranging from cancer to normal endometrium. Endometrial hyperplasia and disorganized proliferative endometrium were the next most common symptoms in patients with AUB after normal cyclic endometrium. Endometrial lesions were associated with particular ages. The age range of 31 to 40 years was where normal cycle proliferative endometrium was most frequently detected. The age group of 41 to 50 years old had a significant incidence of endometrial hyperplasia, disorganized proliferative endometrium, and endometrial polyp. After the age group of 50, endometrial cancer incidence was significant. These findings unmistakably demonstrated that a histological examination is necessary in every case of AUB in order to rule out preneoplastic or malignant lesions. Gynecologists can benefit greatly from this straightforward investigation of endometrial curettage or biopsy in order to plan treatment for a patient with AUB through attentive monitoring of a patient who has a precursor lesion or through prompt surgical intervention in the case of malignant lesions. Younger women made up a sizable subset of those with abnormal uterine bleeding brought on by abortion. Therefore, any patient with AUB who is in the reproductive age group should have the possibility of pregnancy difficulties ruled out. In a few cases, chronic endometritis was discovered. Epithelioid granulomas in one case suggested TB. AUB, pelvic discomfort, and infertility are symptoms that patients with chronic endometritis may experience. since of a specific treatment, this ailment requires a diagnosis since the endometrium returns to its natural state.

CONCLUSION:

AUB is brought on by age-related disease in the endometrium. AUB is evaluated using endometrial biopsy histopathology as a key diagnostic technique, and a definite diagnosis could aid the doctor in formulating a treatment strategy for the effective management of AUB. Endometrial biopsy and curettage histopathological patterns in women

with AUB are varied. These lesions range from straightforward physiological to incredibly complex pathological ones. The vast majority of the lesions causing AUB found in this investigation were fetal lesions, which are most frequently found in female reproductive patients. However, perimenopausal women frequently experienced endometrial hyperplasia, and both perimenopausal and postmenopausal women occasionally developed endometrial cancer.

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