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TO STUDY THE HISTOMORPHOLOGICAL PATTERNS OF ENDOMETRIUM IN ABNORMAL UTERINE BLEEDING

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ABSTRACT

BACKGROUND: The gold standard diagnostic method for abnormal uterine bleeding is an endometrial histopathology examination. This condition is widespread in gynecological complaints. One of the most prevalent gynecological problems affecting women worldwide is endometrial disease. These illnesses affect people of all ages and have a substantial negative impact on the morbidity and mortality rates of mothers. The majority of female endometrial disease patients initially exhibit abnormal uterine bleeding (AUB). AUB thus supports the requirement for an immediate diagnosis. This is due to the large variety of endometrial disease histological patterns. Simple endometrial hyperplasia to more complicated conditions like endometrial cancer is among these lesions. Diagnosing most of these lesions requires taking an endometrial sample. For a conclusive identification of the lesions, the two most crucial sample techniques are curettage and endometrial biopsy. Women with this menstruation illness are affected from adolescence through postmenopause. AUB is characterized by variations in the amount of blood flow, length, frequency, or intermenstrual bleeding.

AIM: The purpose of this study is to examine different endometrial histomorphological patterns in patients with abnormal uterine bleeding from a range of age groups.

MATERIAL AND METHOD: This study looked back at patients who had presented to the Department of Pathology with AUB during that time. In this investigation, the pathology department examined 120 samples of endometrial curettage tissues with clinical symptoms of abnormal uterine hemorrhage for histological evaluation. Women presenting with AUB provided endometrial samples to the Department of Pathology via fractional curettage, endometrial biopsy, and dilatation and curettage (D and C). The Department of Pathology provided the histopathological reports on each of these instances, while the Department of Medical Records provided further information about the patients. Medical records were used to gather information on the patient's demographics, parity, gestational age if she was pregnant, indication, and histopathology results.

RESULTS: The study comprised 120 endometrial curetts in total. With a mean age of 40.4 years, the patients with AUB range in age from 18 to 79 years. The age range of 40 to 49 years old had the highest frequency of AUB. Proliferative endometrium was the most prevalent finding in women under 40, followed by secretory endometrium and disordered proliferative endometrium. A disorganized proliferation pattern was seen in 12 cases (10%), with the age groups of 30 to 39 and 40 to 49 years old showing the highest prevalence of this pattern. Four (3.4%) of the lesions were found to be malignant.

CONCLUSION: What makes up the largest percentage of histopathological findings are normal cyclic changes. On the other hand, hyperplasia and cancers are significant contributors to bleeding during and after menopause. Although the effectiveness of D&C in diagnosing premalignant and malignant cases is still dubious, its usage as a sampling method for AUB patients is still widely used. In order to rule out preneoplasia and cancer, patients experiencing abnormal uterine bleeding should have endometrial samples examined histopathologically. Physiological features such as proliferative

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endometrium, secretory endometrium, and monthly fluctuations were normal in patients without organic pathology.

KEYWORDS: Abnormal uterine bleeding, Histopathology, Endometrial hyperplasia and Carcinoma

Introduction:

The symptom known as abnormal uterine bleeding (AUB) is a departure from the typical menstrual cycle. Variations in the menstrual flow's frequency, volume, and duration are associated with AUB.[1] Bleeding after a year of no menstruation is considered postmenopausal in women.[2] It is challenging to ascertain the prevalence of this symptom since women might not seek medical attention, and doctors might rely on the patient's subjective assessment of their symptoms, which does not satisfy objective standards. The estimated prevalence of AUB, a more general term, exceeds 10%–30% since heavy menstrual bleeding affects around 10%–30% of women who are of reproductive age. Subscales measuring the physical and emotional aspects of role functioning reveal the full impact of AUB, which hinders everyday activities and work productivity.[3] Prolonged bleeding can have negative medical and social effects on a woman's health, leading to chronic sickness in developing countries and iron deficiency in developed countries.[4] AUB include bleeding from structural causes such as fibroids, polyps, endometrial cancer, and problems during pregnancy, as well as dysfunctional uterine bleeding (DUB).[5] DUB is defined as AUB without a demonstrable organic cause.[6] In most instances DUB is due to the occurrence of an anovulatory cycle.[7]

The initial step in treating AUB, which has an age-related etiology, is to rule out pregnancy-related reasons using the patient's medical history and the presence of the human chorionic gonadotropin b-subunit.[8] The International Federation of Gynecology and Obstetrics (FIGO) has proposed the PALMCOEIN classification, which, after ruling out pregnancy, focuses on causes by structural pathologies (Polyps, Adenomyosis, Leiomyomas, and Malignancy or atypical endometrial hyperplasia [PALM]). On the other hand, the causes classified as "COEIN" are non-structural and are diagnosed using a broader range of clinical assessment, history, and occasionally laboratory tests (Coagulopathies, Ovulatory disorders, primary Endometrial disorders, Iatrogenic and Not otherwise classified; COEIN).[2] Histological changes in the endometrium, which account for the woman's age, menstrual cycle phase, and use of any exogenous hormones, can reveal the underlying disease. For women who are perimenopausal or postmenopausal, an early evaluation is crucial in order to determine the precise type of the lesion and rule out cancer.[9] Research has indicated that the age of patients has an impact on the histological patterns of diagnosis.[10] The majority of young women who are fertile typically exhibit changes linked to an imbalance in hormones more frequently. Nonetheless, endometrial hyperplasia and endometrial cancer are more common in older women in the premenopausal and postmenopausal age groups.[11] According to reports, endometrial cancer ranks second in developing nations behind cervix cancer in terms of frequency of gynecological malignancies, while it is the most prevalent in industrialized nations. According to research conducted in the US, endometrial cancer accounts for 6% of all gynecological cancer cases and is the third most common cause of death from gynecological cancer, after cervical and ovarian cancers.[12] Endometrial cancer is found in around 10% of perimenopausal and postmenopausal women with AUB worldwide.[13] The gold standard diagnostic method for evaluating AUB is the histopathological analysis of endometrial samples. A precise diagnosis aids in the planning of the therapy for effective, creative management of AUB, where hormone interaction is the key to successful treatment rather than hysterectomy.[14] In women who

experience menorrhagia, it is crucial to rule out two significant pathologies: endometrial cancer and hyperplasia. The study's objectives were to: (a) comprehend the Histopathological Examination (HPE) of endometrial tissue in patients with abnormal uterine bleeding; and (b) compare the HPE results in AUB across various age groups.

MATERIAL AND METHODS

This study looked back at patients who had presented to the Department of Pathology with AUB during that time. In this investigation, the pathology department examined 120 samples of endometrial curettage tissues with clinical symptoms of abnormal uterine hemorrhage for histological evaluation. Women presenting with AUB provided endometrial samples to the Department of Pathology via fractional curettage, endometrial biopsy, and dilatation and curettage (D and C). The Department of Pathology provided the histopathological reports on each of these instances, while the Department of Medical Records provided further information about the patients. Medical records were used to gather information on the patient's demographics, parity, gestational age if she was pregnant, indication, and histopathology results. Patients were divided into age groups and parity categories. Since this retrospective chart review entailed the viewing and analysis of de-identified data from electronic medical records, patient permission was waived.

Inclusion criteria:

- Women presented with AUB in all age groups.

Exclusion criteria:

- Patients with bleeding due to leiomyomas, cervical pathology, pregnancy-related complications, and hemostatic disorders were excluded from the study.

Specimen sampling and laboratory procedure

Inpatient settings saw the use of dilatation and evacuation (D&E) or D&C under hysteroscopy for biopsies. After passing the sound to determine the length and orientation of the uterus, the cervix dilates during a D&C procedure. The cervix is already dilated in D&E. After the uterus has sufficiently dilated, the specimen is collected in a container containing 10% formalin and transported to the pathology lab for processing. The sharp end of the curette is passed across the anterior, posterior, two lateral, and finally the fundus of the uterus. To create the pathology slides, the endometrial tissues were fixed in 10% formalin. Hematoxylin and eosin stain was used after the tissues fixed in paraffin were sectioned. Pathologists examined sections under a light microscope. Age and tumor kind were taken into consideration when analyzing the data. When required, special stains such as periodic acid Schiff stains and reticulin were used.

The AUB histopathology results were divided into organic and functional reasons. The proliferative and secretory phases of the normal cycle endometrium, as well as other aberrant changes 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, endometrial hyperplasia, endometrial cancer, benign endometrial polyp, endometrial stromal nodule, and chronic endometritis were the organic intrauterine lesions that caused AUB. A thorough histological analysis was done, and the results were recorded. The histological results from the hysterectomy specimens were compared with the D&C histological findings, which are regarded as the current best practice, in order to assess the diagnostic accuracy. The gathered information was divided into groups according to the different endometrial morphologies, and the age distribution within each group was examined.

STATISTICAL ANALYSIS

Descriptive statistics such as mean, SD, and percentage were used. A statistical analysis between age and specific endometrial causes was done using a chi-square test. The data was entered in statistics software i.e., Statistical Package for Social Sciences (SPSS) version 17, and descriptive analysis of age, and type of lesion was done.

RESULT: -

A total of 120 endometrial curetts were included in the study. The age of the patients

with AUB ranges from 18 to 79 years, with a mean of 40.4 years. The highest incidence of AUB was found in the age group of 40 to 49 years.

Table 1: Age-wise distribution of cases

Age groups (years)	N	%
Less than 20	2	1.6
20-29	19	15.8
30-39	25	20.8
40-49	45	37.5
50-59	15	12.5
60-69	10	8.3
70-79	04	3.3

Proliferative endometrium was the most prevalent finding in women under 40, followed by secretory endometrium and disordered proliferative endometrium. A disorganized proliferation pattern was seen in 12 cases (10%), with the age groups of 30 to 39 and 40 to 49 years old showing the highest prevalence of this pattern.

Table 2: Histopathological picture of the endometrium

Endometrium pattern	N	%
Proliferative endometrium	32	26.6
Secretory endometrium	12	10
Pill endometrium	10	8.3
Atrophic endometrium	12	10
Endometritis	3	2.5
Endometrial polyp	4	3.3
Simple cystic hyperplasia	11	9.1
Adenomatous hyperplasia	3	2.5
Disordered proliferation	17	14.1
Complex hyperplasia without atypia	2	1.6
Complex hyperplasia with atypia	4	3.3
Endometrial carcinoma	8	6.6
Others	2	1.6

Table 2 shows histopathology findings of the endometrial biopsy, The maximum case was proliferative endometrium (26.6%) was the maximum case followed by disordered proliferation (14.1%) Others which include pregnancy complications and squamous cell carcinoma comprised 1.6% of the cases. The most common finding was normal cyclical pattern endometrium, showing proliferative endometrium in 26.6% and secretory endometrium in 10% of our cases.

Atrophic endometrium was seen in 12 patients mostly of post-menopausal age group, but some women in the age group of 40 to 49 show atrophic endometrium. Carcinoma endometrium was seen in 8 cases out of which 70% are above the age group of 50. But carcinoma endometrium was found in one patient of 35 years, who had a history of ovulation and diabetes mellitus type 2. The incidence of endometrial hyperplasia in our study was 10% and endometrial carcinoma was 6.6%. The incidence of endometrial hyperplasia and endometrial carcinoma was highest after the 4th decade of life suggesting that the incidence of endometrial hyperplasia and endometrial carcinoma increases with age.

Table 3: Types of lesions in endometrial curettage specimen

Lesion type	*No of lesion*	*Percentage*
Benign	***116***	***96.6***
Malignant	***04***	***3.4***
	120	***100%***

It was noted that 4 (3.4%) were having malignant lesions.

DISCUSSION

The endometrium is a woman's hormone status mirror. Endometrial histological variation can be observed based on a woman's age, the stage of her menstrual cycle, and any other unique pathology.[15] In a typical cycle, endometrial growth stimulated by estrogen takes place after monthly shedding. The endometrial glands enlarge and become twisted during this stage.[16] On the ninth postovulatory day, the spiral arterioles arise as a result of endothelial proliferation, wall thickening, and coiling, which are characteristics of the secretory activity in the second part of the menstrual cycle.[17] Numerous physiological, pathological, or pharmacological factors can produce AUB, which has significant social and health consequences. A thorough history and physical examination, as well as laboratory tests involving imaging and endometrial sampling, are necessary for the evaluation of AUB.[5,18] The total blood count, platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT), and liver function test are among the standard noninvasive tests performed for atypical uterine bleeding. Follicle-stimulating hormone (FSH), prolactin estimation, thyroid function tests, and luteinizing hormone (LH) must be used to rule out endocrine abnormalities and pregnancy in women of reproductive age. Tissue samples and transvaginal sonography are performed once these causes have been ruled out. Both therapeutic and diagnostic operations can be achieved through dilatation and curettage.[5]

Specifically, studies by **Jairajpuri et al.2013**[19] found 35.9% of AUB cases in women in their fifth decades. Again, other studies revealed as high as 48.1% of AUB cases in women in their fifth decades.[20] **Vaydia et al.2013**[21] in their study reported 40.94% cases of normal endometrium, 13.40% cases of disordered proliferative endometrium, 10.92% cases of endometrial hyperplasia, and 2.88% cases of endometrial cancer. **Dwivedi et al.2019**[22] also found in their study normal menstrual pattern in 48.15% of cases, hormonal and pill effects in 22.22% of cases, endometrial hyperplasia in 3.70% of cases, endometrial cancer in 1.85%.

Mirza et al.2011[23] examined endometrial tissue of 1000 cases of AUB and reported a normal cyclical pattern in 35.06%, disordered proliferation in 22.80%, 30% endometrial hyperplasia, and 2% endometrial carcinoma, and 7% atrophic endometrium. **Doraiswami et al.2012**[24] in a study of 409 cases of AUB noted normal cyclical endometrium in 28.36%, disordered proliferation in 20.54%, most commonly in the age group of 41-50 years of age, pregnancy complication in 22.74% cases and endometrial hyperplasia in 6.11%. **Vani et al.2019**[25] did a study of 231 endometrial biopsies, and found proliferative endometrium in 30.3%, secretory endometrium in 25.97%, disordered proliferation in 5.62%, endometrial polyp in 2.16%, endometrial hyperplasia in 20.09%, pill endometrium in 2.0%, and endometrial cancer in 0.86%.

An significant contributing factor to AUB is endometrial hyperplasia, which is characterized by an elevated gland-to-stroma ratio due to the endometrial glands' greater proliferation in comparison to the stroma. Given the connection between endometrial hyperplasia and endometrial cancer, this condition warrants special consideration. The World Health Organization (WHO), which was first put forth by Kurman & Norris, split endometrial hyperplasia into two categories: simple and complicated. Each category was then further separated into typical and atypical categories based on cytology.[26] The percentage of simple hyperplasia and complicated hyperplasia that

develops to carcinoma is 1% and 3%, respectively, in cases without cytological atypia and 29% and 8%, respectively, in cases with cytological atypia. As a result, classifying endometrial hyperplasia into typical and atypical forms has therapeutic and prognosis significance, with atypical varieties showing a higher risk of developing into cancer.[27] Given the significant morphologic overlap between complicated hyperplasia with atypia and well-differentiated endometrioid adenocarcinoma, it may not be possible to distinguish between the two conditions with certainty. A hysterectomy cannot be justified by the mere existence of hyperplasia. Hormonal therapy and refraining from hysterectomy are the main treatments for endometrial hyperplasia.

As the gold standard diagnostic method for evaluating AUB, histopathological examination of endometrial samples reveals a range of patterns from normal endometrium to cancer. Normal cyclic endometrium was the most common presentation in most AUB patients, followed by endometrial hyperplasia and disorganized proliferative endometrium. Endometrial lesions had an age-specific correlation. These findings unequivocally demonstrate that, in order to rule out preneoplastic or malignant lesions, a histological examination is required in every instance of AUB. Gynecologists can benefit greatly from this straightforward research of endometrial curettage or biopsy when planning the course of treatment for a patient with AUB. This can involve closely monitoring a patient who has a precursor lesion or, in the event of malignant lesions, prompt surgical intervention.

CONCLUSION:

There is a specific age inclination for the causes of abnormal uterine bleeding, and AUB can be concerning at any age. Early diagnosis of precancerous endometrial lesions and malignancies can be facilitated by endometrial biopsy and histological assessment. According to this study, endometrial hyperplasia was found in the perimenopausal age range and a significant percentage of endometrial cancer was found in the postmenopausal age group with AUB. For the purpose of correctly diagnosing and treating AUB in women of all ages, it is crucial to evaluate endometrial patterns in any age group. It is the primary diagnostic technique used to assess AUB since it displays a broad range of patterns, from a healthy endometrium to cancer. Thus, it lessens the need for a needless hysterectomy and aids the doctor in formulating a treatment plan for the effective care of AUB.

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