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ENDOMETRIAL ENIGMAS: A HISTOPATHOLOGICAL EXPLORATION OF ABNORMAL UTERINE BLEEDING IN WOMEN PRESENTING IN TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) affects 10-20% of reproductive-age women, strongly impacting quality of life and reproductive health. Endometrial biopsy is crucial for diagnosing underlying pathologies. Various studies report differing histopathological findings with limited data on specific populations, highlighting the need for comprehensive data.

Objective/s:
To determine the histopathological pattern of endometrial biopsies performed in women presenting with abnormal uterine bleeding & to analyze the frequency of various histopathology patterns identified.

Study settings: Cross-sectional study conducted at Department of Obstetrics & Gynecology, Central Park Teaching Hospital, Lahore from 15-06-2023 to 14-12-2023

Methodology: One hundred and fifty females with abnormal uterine bleeding were enrolled who underwent biopsy by dilation and curettage. Findings of histopathological reports were recorded. Data was analyzed in SPSS ver. 26.

Results: The current study showed that participants' mean age was 46.23 ± 17.18 years. The most common complaints of abnormal uterine bleeding were post-menopausal bleeding (33.3%), heavy irregular menstrual bleeding (33.3%), and cyclical heavy bleeding (18.7%). The most common pathology was functional endometrium (50%), followed by endometrial atrophy (14.0%), benign lesions (11.3%), malignant lesions (7.3%), inflammatory endometrium (1.3%), and few others were observed in 16% cases.

Conclusion: The most common pathology in local population observed on histopathology was functional endometrium, while malignant lesions were less frequent.

Key words: Abnormal uterine bleeding, endometrial biopsies, histopathological pattern, hyperplasia, malignancy, functional endometrium

INTRODUCTION

Abnormal uterine bleeding (AUB) is a pervasive gynecological complaint affecting millions of women worldwide, impacting the quality of life, reproductive health, and mental well-being. AUB is a comprehensive phrase used to describe deviations from the typical menstrual cycle, including variations in the frequency, regularity, duration, and amount of flow, excluding cases of pregnancy that encompass various bleeding patterns, including heavy menstrual bleeding, irregular menstrual bleeding, intermenstrual bleeding, and postmenopausal bleeding. The etiology of AUB is complex, involving hormonal imbalances, uterine anatomical abnormalities, systemic diseases, and neoplastic conditions.

Endometrial biopsy is a vital diagnostic tool for evaluating AUB, providing valuable histopathological information essential for accurate diagnosis, risk stratification, and personalized treatment. The histopathological examination of endometrial tissue can reveal various pathologies, including endometrial hyperplasia, endometrial polyps, leiomyomas, and endometrial cancer.
Understanding the histopathological patterns of endometrial biopsies in women with AUB is crucial for optimizing patient care. However, existing literature highlights significant variability in reported histopathological findings, underscoring the need for comprehensive studies additionally endometrial tissue sampling is not universally required for all women experiencing abnormal uterine bleeding, but in women who are at a high risk of developing hyperplasia or cancer.

Around one-third of women may have abnormal uterine bleeding at some stage in their lives, with abnormalities often occurring between the commencement of menstruation and the transition to menopause. A typical menstrual cycle has a frequency of 24 to 38 days and a duration of 2 to 7 days. During this period, the quantity of blood loss varies between 5 and 80 millilitres. Any variations from these four criteria are classified as abnormal uterine haemorrhage.[1]

Abnormal uterine bleeding may be classified as either acute or chronic. Acute abnormal uterine bleeding is a disorder characterised by heavy and urgent bleeding that requires immediate intervention to avoid further blood loss. Acute abnormal uterine bleeding may occur by itself or with chronic abnormal uterine bleeding, which refers to abnormalities in monthly bleeding over most of the last 6 months[2]. The prevalence of abnormal uterine bleeding in women of reproductive age worldwide is believed to vary between 10% and 30%[3], with a greater incidence noted between the initiation of menstruation and the shift towards menopause. The focus of many studies is limited to heavy menstrual bleeding (HMB). However, some studies suggest a much higher incidence[3.]

Endometrial tissue sampling is not universally required for all women experiencing abnormal uterine bleeding, however it is recommended for women who have a high risk of developing hyperplasia or cancer. An endometrial biopsy is the primary diagnostic test recommended for women aged 45 or above experiencing abnormal uterine bleeding. Endometrial sampling is recommended for women under the age of 45 who have unopposed estrogen exposure, such as those with obesity and/or polycystic ovarian syndrome, and who have not responded to treatment or continue to experience chronic bleeding.[4-6.]
Therefore this study was planned to be done in local setting to attain the most common pathology causing abnormal uterine bleeding in local population.

OBJECTIVE/S:

1. To determine the histopathological pattern of endometrial biopsies performed in women presenting with abnormal uterine bleeding
2. To analyze the frequency of various histopathology patterns identified.

MATERIAL AND METHODS

Study design: Cross-sectional study

Study place and duration: Department of Obstetrics & gynecology, Central Park Teaching hospital, Lahore from 15-06-2023 to 14-12-2023

Sample size: Sample size for this research was calculated as 150 cases by keeping 95% confidence level, 5% absolute precision required and percentage of hyperplasia i.e. 10.92% in females with abnormal uterine bleeding.

Sampling technique: Non-probability, consecutive sampling technique was applied to include the females in the study who fulfilled following selection criteria.

Selection criteria: Females diagnosed with abnormal uterine bleeding, fall in age range above 18 years were enrolled, either married or unmarried were enrolled in the study. Females already diagnosed with endometrial or ovarian pathology were excluded. Females with recurrent disease or already under process of treatment, taking chemotherapy for malignancy or metastatic diseases were excluded. Inadequate samples were also excluded from the study

Data collection: One hundred and fifty females with abnormal uterine bleeding were enrolled from emergency department. Informed consent was taken before enrolment and demographic information including name, age, body mass index, marital status, history of smoking, diabetes, use of family history of abnormal uterine bleeding or endometrial or ovarian pathology, previous gynecological treatment (if taken any), number of vaginal deliveries, were noted. Then females will be admitted and planned for biopsy through dilation and curettage. Samples were obtained and stored carefully and transferred to pathology department for histopathological review. Reports were assessed and findings were recorded and discussed with senior pathologist. Findings including Proliferative phase, Secretory phase, Simple hyperplasia, Complex hyperplasia, Atypical hyperplasia, Endometritis, Endometrial Carcinoma, Metastatic Carcinoma, Atrophic Endometrium were noted.

Data analysis: All the data was analysed in SPSS ver. 26.

RESULTS

In this study, the mean age of females was 46.23 ± 17.18 years. Out of 150 females, 72 (48.0%) had age between 18-39 years, 29 (19.3%) had age 40-50 years and 49 (32.7%) had age >50 years. There were 143 (95.3%) married females while 7 (4.7%) were unmarried and nulliparous, 10 (6.7%) were primiparous and 133 (88.7%) were multiparous. The mean body mass index of females was 30.67 ± 6.29 kg/m^2. Out of 150 females, 108 (72.0%) were obese, 7 (4.7%) had history of smoking, 52 (34.7%) had diabetes mellitus. Family history of abnormal uterine bleeding was positive in 36 (24.0%) females, while family history of endometrial or uterine pathology was positive in 20 (13.3%) females, previous history of gynecological procedure was positive in 60 (40%) females and 70 (46.7%) females had history of vaginal deliveries. The most common complaint of abnormal uterine bleeding was 50 (33.3%) were post-menopausal, 50 (33.3%) had complaint of hey irregular bleeding, 22 (14.7%) had irregular vaginal bleeding (other than menstrual cycle) and 28 (18.7%) had cyclical but heavy bleeding. Table 1

Out of 150 females, the most common pathology was functional endometrium [75 (50%)], followed by endometrial atrophy [21 (14.0%)], benign lesions [17 (11.3%)], malignant lesions [11 (7.3%)] and inflammatory endometrium [2 (1.3%)] and few others were also observed [24 (16.0%)] cases were also observed. Fig 1

In 75 females with functional endometrium, most common pathology was secretory phase [247 (31.3%)], followed by proliferative phase [27 (18.0%)] and disorder proliferative phase [1 (0.7%)].

Out of 21 females with endometrial atrophy, most common pathology was hyperplasia without atypia [11 (7.3%)], followed by atrophic endometrium [8 (5.3%)], and endometrial hyperplasia [2 (1.3%)]. Out of 17 females with benign lesions, most common pathology was benign endometrial polyp [14 (9.3%)] and leiomyoma [3 (2.0%)]. Out of 11 females with malignant lesions, most common pathology was endometrioid adenocarcinoma [7 (4.7%)], followed by mixed mullerian tumour [2 (1.3%)], serous carcinoma [1 (0.7%)] and endometrial stromal neoplasm [1 (0.7%)]. Out of 2 females with inflammatory endometrium, acute endometritis was noted [2 (1.3%)] females. Hormonal effect was noted in 10 (6.7%) and 7 (4.7%) females had autolyzed endometrium. Table 2

Table 1: Basic demographics of females enrolled in the study

Features	F (%), mean ± SD
n	150
Age (years)	46.23 ± 17.18
18 -39 years	72 (48.0%)
40- 50 years	29 (19.3%)
>50 years	49 (32.7%)
Marital status	
Married	143 (95.3%)
Unmarried	7 (4.7%)
Parity	
Nulliparous (unmarried)	7 (4.7%)
Primiparous	10 (6.7%)
Multiparous	133 (88.7%)
Body mass index (kg/m^2)	30.67 ± 6.29
Risk factors:	
Obesity	108 (72.0%)
Smoking	7 (4.7%)
Diabetes mellitus	52 (34.7%)
Family history of abnormal uterine bleeding	36 (24.0%)
Family history of uterine or endometrial pathology	20 (13.3%)
Previous history of gynaecological treatment	60 (40%)
Previous vaginal delivery	70 (46.7%)
Presenting complaint	
Heavy regular vaginal bleeding	28 (18.7%)
Heavy irregular vaginal bleeding	50 (33.3%)
Irregular vaginal bleeding	22 (14.7%)
Postmenopausal bleeding	50 (33.3%)

Fig 1: Distribution of histopathological findings

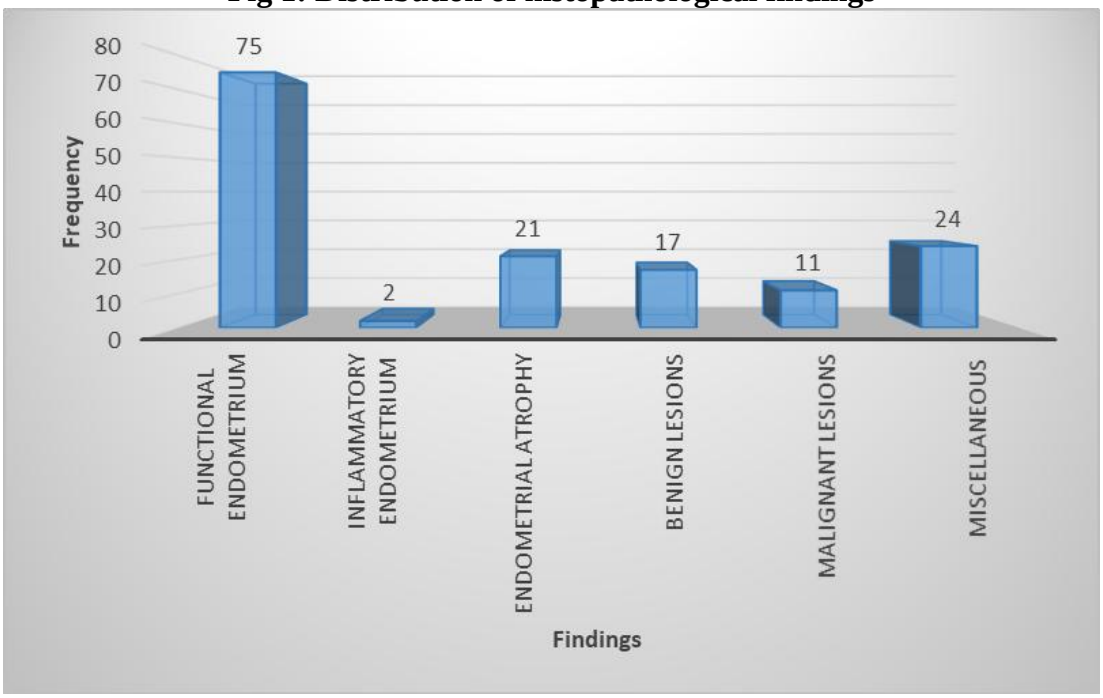

Table 2: Distribution of subtype of histopathological findings

Histopathological finding	F (%)
Functional endometrium	75 (50.0%)
• Proliferative phase	27 (18.0%)
• Secretory phase	47 (31.3%)
• Disordered proliferative phase	1 (0.7%)
Endometrial atrophy	21 (14.0%)
• Atrophic endometrium	8 (5.3%)
• Endometrial hyperplasia	2 (1.3%)
• Hyperplasia without atypia	11 (7.3%)
• Atypical hyperplasia	0 (0%)
Benign lesions	17 (11.3%)
• Benign endometrial polyp	14 (9.3%)
• Leiomyoma	3 (2.0%)
Malignant lesions	11 (7.3%)
• Endometrioid adenocarcinoma	7 (4.7%)
• Serous carcinoma	1 (0.7%)
• Mixed mullerian tumour	2 (1.3%)
• Endometrial stromal neoplasm	1 (0.7%)
Inflammatory endometrium	2 (1.3%)
• Acute Endometritis	2 (1.3%)
• Chronic nonspecific endometritis	0 (0%)
• Granulomatous endometritis	0 (0%)
Miscellaneous	24 (16.0%)
• Inactive endometrium	2 (1.3%)
• Hormonal effect	10 (6.7%)
• Autolyzed endometrium	7 (4.7%)
• Unidentified/inadequate	5 (3.3%)

DISCUSSION

Abnormal uterine bleeding, seen in a uterus that is physically normal, with regular monthly cycles and no signs of coagulopathy, is most likely due to an underlying problem in the endometrium. The comprehension of endometrial function during menstruation and associated diseases remains limited and is now being studied by scientists. The precise cascade of events triggered by the cessation of progesterone due to the decrease of the corpus luteum in the absence of pregnancy is still not completely understood. Hypoxia, inflammation, haemostasis, and angiogenesis are vital elements in the shedding and postliminary formation of a regenerated superficial layer of the endometrium, which is responsible for its functions. Improper uterine bleeding is linked to decrease in clot strength and integrity due to the breakdown of fibrin results in an increased blood loss during menstruation. Plasminogen activators are fibrinolytic that induce dissolution of blood clots and endometrial and menstrual secretion levels of plasminogen activators are increased in women with menorrhagia.[7]

Endometrial illnesses are prevalent gynecological disorders that have a global impact on women. These disorders affect people of all ages and greatly contribute to higher rates of illness and death among mothers. The prompt diagnosis and therapy are crucial due to the extensive variety of histopathological findings.[8] The histological pattern of endometrial sample, in conjunction with clinical and radiological findings, is the established diagnostic criterion for the clinical diagnosis of endometrial pathology. This information is pivotal in governing the appropriate care for patients.[9]

In our study, out of 150 females, the most common pathology was functional endometrium [75 (50%)]. In 75 females with functional endometrium, most common pathology was secretory phase [247 (31.3%)], followed by proliferative phase [27 (18.0%)] and disorder proliferative phase [1 (0.7%)]. Out of 21 females with endometrial atrophy, most common pathology was hyperplasia without atypia [11 (7.3%)], followed by atrophic endometrium [8 (5.3%)], and endometrial hyperplasia [2 (1.3%)]. Out of 17 females with benign lesions, most common pathology was benign endometrial polyp [14 (9.3%)] and leiomyoma [3 (2.0%)]. Out of 11 females with malignant lesions, most common pathology was endometrioid adenocarcinoma [7 (4.7%)], followed by mixed mullerian tumour [2 (1.3%)], serous carcinoma [1 (0.7%)] and endometrial stromal neoplasm [1 (0.7%)].
A study conducted in Pakistan in 2017 found that the prevailing pathological pattern observed was Proliferative phase endometrium in 16.7%, secretory phase endometrium 14.7%, disordered proliferative endometrium in 16%, atrophic endometrium in 3.3%, chronic endometritis in 16 %, endometrial polyps in 8.7%, endometrial hyperplasia in 12%, endometrial carcinoma in 2%, hormone induced changes in 9.3% and squamous metaplasia was seen in 1.3% .[10]

According to another study conducted in Pakistan, it was found that among women in the premenopausal age range, the most common observation was the presence of proliferative endometrium (48%), followed by secretory endometrium (31%). Among the perimenopausal group, the most prevalent observation was simple hyperplasia, accounting for 41% of cases. Subsequently, proliferative endometrium occurred, accounting for 29% of the cases, and secretory endometrium, accounting for 17% of the cases. Among women in the postmenopausal age group, the most prevalent condition was complex hyperplasia, observed in 33.3% of cases, followed by atrophic endometrium in 27% of instances.[11]

In a comparable study conducted by Shukla et al., it was discovered that Endometrial proliferative pattern was the most common histopathological finding and was seen in 27% patients, followed by endometrial hyperplasia observed in 13.5% patients, while secretory endometrium in (12.7%) and disordered proliferative endometrium were seen in 10.9% participants each. Malignancy was detected in 1.7% of cases and endometrial carcinoma was found the most common lesion.[12]

In a separate study conducted in India, the most frequently detected histological pattern was the usual cyclical patterns, specifically proliferative endometrium (38.8%), secretory phase endometrium (16.3%).[13]

The predominant pattern seen in another Indian study was normal cycling endometrium , accounting for 33.9% of cases. The endometrial hyperplasia (22.2%) identified as commonest pattern. Other causes were disordered proliferative endometrium (13.7%), atrophic endometrium(13.2%), benign endometrial polyp(8%), deficient secretory phase(3.3%), chronic endometritis(2.4%), and endometrial carcinoma(2.3%).[14]

The RCOG guidelines have emphasized this point, except for cases of treatment failure, where the age for sample might be reduced to 40.[15] Other guidelines recommend direct referral for endometrial sampling in high risk women e.g. older[16]. Given the significant rise in endometrial cancer, the authors strongly urge gynecologists to consistently exercise their clinical expertise when evaluating women under the age of 40 who experience excessive monthly bleeding and possess risk factors for precancerous changes, such as obesity and PCOS. Performing endometrial sampling can be more difficult when fibroids cause distortion in the cavity. However, having access to concurrent outpatient hysteroscopy can help in promptly ruling out any endometrial pathology.

For cases of abnormal uterine bleeding without pressure sensations, medical therapy may be preferable, especially when there is a need to preserve fertility. Tranexamic acid and NSAIDs, such as mefenamic acid, are the sole medicinal alternatives that do not have contraceptive effects.[17] Although the risk of expulsion of a levonorgestrel-releasing intrauterine device (LNG IUS) is indeed increased when fibroids are present, there is still data supporting its effectiveness. However, the deformation of the uterine cavity caused by fibroids may make the use of LNG IUS impractical, so evidence from previous studies is inconclusive regarding it's use for menorrhagia due to uterine fibroids.[18] Endometrial evaluation with endometrial biopsy or curettage is recommended for females in the peri and postmenopausal years to rule out the presence of endometrial hyperplasia or cancer. Endometrial sample may be necessary for younger women if irregular bleeding persists despite medical treatment.[19]

The key to successful clinical management is to identify the causative factors responsible. The first aim of the clinician is to restore the cyclic menses of normal volume and duration. This is achieved by thorough clinical examination, ultrasonography and histopathological examination. When no organic cause is evident to clinician, histopathological examination remains the only alternative to reach the diagnosis, and plan for appropriate management.[20] The histopathological diagnosis differs according to age, with an increased incidence of endometrial hyperplasia and cancer detected in perimenopausal and postmenopausal women. Conversely, in younger age groups, alterations associated with hormonal imbalance, infections, hemostatic disorders appear to be more prevalent.[21]

The prevalence of endometrial polyps among women undergoing endometrial biopsy or hysterectomy is between 10-25%. The incidence of these polyps increases with age, reaching its highest point in the fifth decade of life, and gradually decreases after menopause.[22-24] There is no conclusive data indicating that polypoid endometrium has a higher likelihood of undergoing malignant transformation compared to the neighboring normal endometrium.[25]

In our investigation on chronic endometritis, we observed a greater detection rate in the age group of 40-51 (7.2%), followed by the age group of 19-39 (6.3%), and the age group above 52 (4.3%). These figures exhibit a substantially lower magnitude as compared to the previously reported figures.[26] Possible factors in our configuration may include partial abortions, which are prevalent and often lead to endometritis.

Insufficient samples are reported when there is a failure to obtain a specimen or when the quality or amount of tissue in a sample is not enough for a proper evaluation. The current study demonstrated a deficiency rate of 9%, which is significantly lower than the findings from prior research study.[27] Postmenopausal women are more likely to experience higher rates of failure and insufficient sampling. This is mostly caused by the prevalence of endometrial atrophy and cervical stenosis causing fluid collection in the endometrial cavity and making it difficult to retrieve the sample.[28] In postmenopausal women, this discovery typically indicates a thinning of the endometrium and an ultrasound measurement of the endometrial thickness that is less than 5 mm. The bleeding in these women is most likely caused by superficial petechial hemorrhages and mucosal ulceration, which result from the delicate vascular support supplied by a thin underlying stroma.

CONCLUSION

The histopathological examination revealed that the most prevalent pathology in the local population was benign, whereas malignant cases were the least common. Endometrial assessment is particularly advised in females who exhibit abnormal uterine bleeding, in order to exclude the potential of any pre-neoplastic condition or malignancy.

CONFLICT OF INTEREST

None

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