

## Endometrial biopsies in females with abnormal uterine bleeding: Clinicopathological analysis

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### Abstract

**Background:** Abnormal Uterine Bleeding (AUB) is a very common complain that drives large number of patients to seek medical advice. Histopathological analysis of endometrial biopsy is the basic mean to diagnose the major causes of AUB. The aim of this study is to analyze a range of histopathological finding in endometrial biopsy obtained from patients presented with AUB to identify most common pathological changes in these biopsies in relation to age.

**Materials and Methods:** A retrospective study of total number of 230 endometrial biopsy was done. The specimens were collected from a private histopathology laboratory in Benghazi during the period from January 2018 to December 2019. The histopathological patterns of endometrial lesions were observed in the different age groups and their frequencies and percentages were computed and analyzed.

**Results:** These studies included patients with age range from 20 to 79 years. The predominant age group with AUB was perimenopausal age group (41-50years). The most common histopathological finding in this study was normal menstrual pattern (27%) followed by simple endometrial hyperplasia (16.5%) and endometrial polyp (16.5%). Other patterns identified were disordered proliferative endometrium (15.2%), irregular hormone response (4%), exogenous hormone changes (2.2%), Arias Stella reaction (3%), inactive endometrium (5.2%), and endometrial carcinoma (7%), and the majority was in >50 years.

**Conclusions:** Histopathological examination of endometrial biopsy obtained by dilation and curettage showed a very large spectrum of endometrial lesions. by classifying these lesions based on age group a large panoramic view was obtained which will help in identify patients with high risk of precancerous lesion.

**Keywords:** abnormal uterine bleeding, disordered proliferative endometrium, endometrial hyperplasia, endometrial polyps, endometrial carcinoma

### Introduction

Normal menstruation is defined as the bleeding from secretory endometrium in non-menopausal women, not exceeding a length of 5 to 10 days with volume of 80-100 ml/menses<sup>[1]</sup>. Abnormal uterine bleeding is a very common gynaecological problem that affects all age groups and the bleeding is considered abnormal when it differs in frequency, duration and amount from normal menstrual cycle or after menopause<sup>[2, 3]</sup>. AUB is associated with functional causes, which is called dysfunctional uterine bleeding, like abnormal physiological changes of endometrium such as inactive endometrium, weakly proliferative endometrium, and disordered proliferative<sup>[4]</sup> or organic causes such as chronic endometritis, hyperplasia, polyp, carcinomas and pregnancy related complications<sup>[4, 5, 6]</sup>. Biopsy obtained by dilation and curettage from patient with AUB is the basic line of diagnosis<sup>[7]</sup>. The aim of this study is to calcify the different histopathological pattern in in all age groups presented with AUB to determine age group at higher risk of premalignant or malignant lesions.

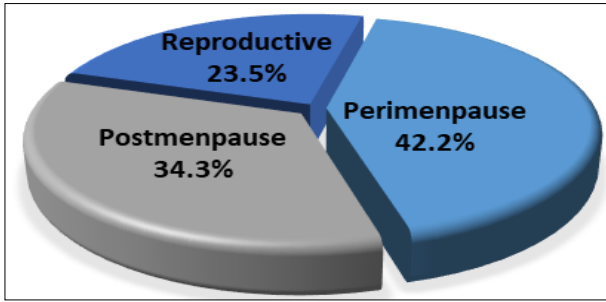
### Materials and Methods

The study was retrospective and it analyzes a total number of 230 endometrial biopsy obtained by dilation and curettage under general anesthesia, to insure adequacy in material. All the Patinates were presenting with abnormal uterine bleeding. The samples were collected from a private histopathology laboratory record. The endometrial samples received was fixed in 10% formalin and routinely processed and stained with Haematoxylin and Eosin (H&E).

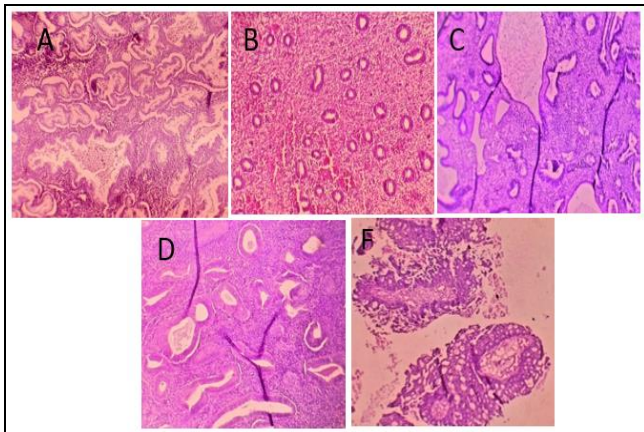
Histopathological examination was done under light microscope. The patients were grouped, based on age in years, into three groups as following: reproductive age (20-40), perimenopausal (41-50), and postmenopausal (>50yrs). The data was presented as mean  $\pm$  SD for age, frequencies and percentages were calculated.

### Results

The mean age of AUB cases included in this study was 48.03 years  $\pm$ 11.02 (20-79 years). The most common age was perimenopausal age group which included (97/230 patients, 42.2%) followed by postmenopausal age group, (79/230 patients, 34.3%) and then reproductive age groups (54/230 patients, 23.5%) (figure 1). The most common histopathological finding in this study was normal menstrual pattern (62/230 cases, 27 %). Amongst these (43/62 cases, 69.4 %) were secretory phase and (19/62 cases, 30.6%) were proliferative phase. The other histological patterns noticed were, benign endometrial polyp (38/230 cases, 16.5%), disordered proliferative endometrium (35/230 cases, 15.2%), irregular hormone response (9/230 cases, 4%), exogenous hormonal response (5/230 cases, 2.2%), inactive endometrium (12/230 cases, 5.2%), Arias Stella reaction (7/230 cases, 3%), simple endometrial hyperplasia (38/230 cases, 16.5%), complex endometrial hyperplasia (8/230 cases, 3.5%), and endometrial carcinoma; endometrial adenocarcinoma and squamous cell carcinoma (13/230 cases, 5.7%, 3/230 cases, 1.3% respectively). Representative pictures of the histopathological finding were demonstrated in figure 2.



**Fig 1: Age distribution of the examined population.** The perimenopause group account for the highest number of cases.



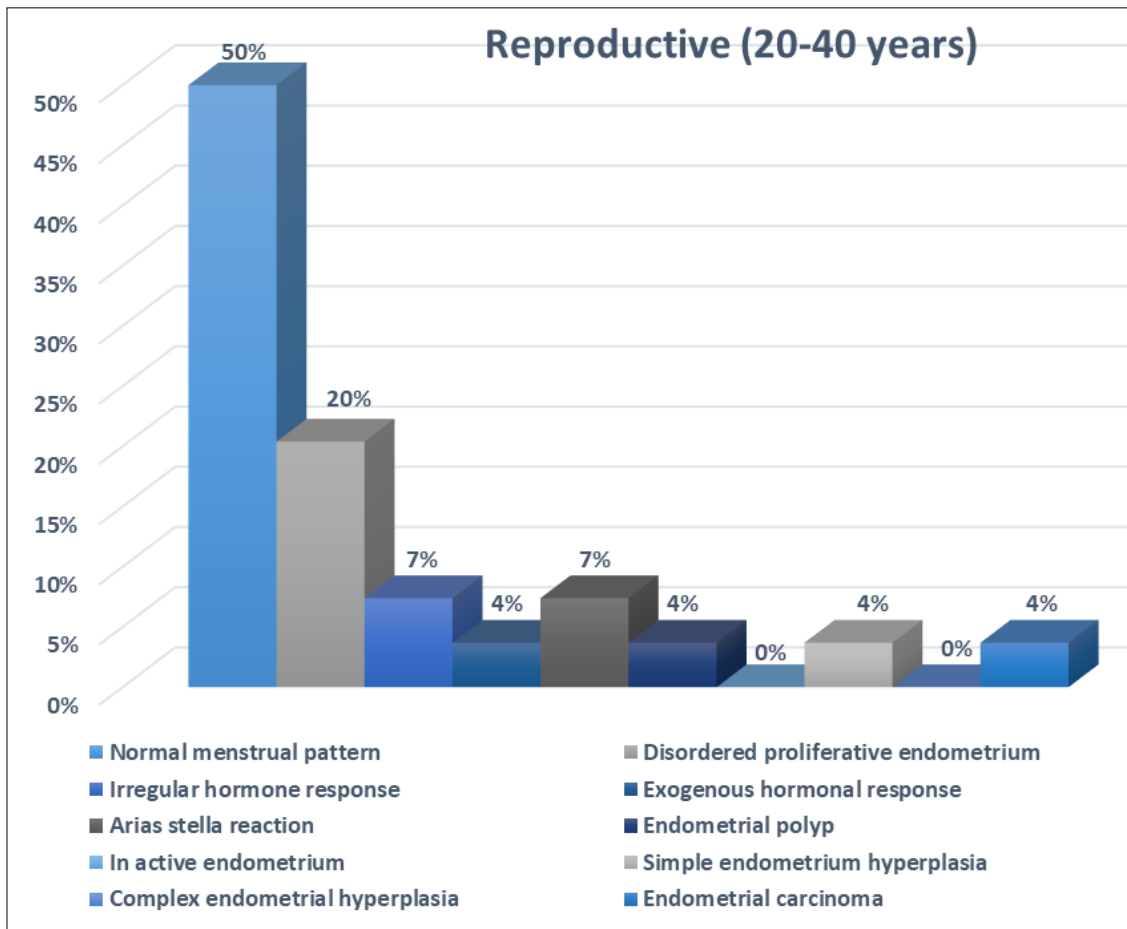
**Fig 2: Different histopathological finding in endometrial biopsy.**

A) Secretory endometrium showing increased luminal secretions and a ragged luminal border of the cells lining (H&E, x100). B) Proliferative endometrium showed straight and tubular glands, having columnar lining with basal nuclei (H&E, x100). C) Endometrial polyp showed dilated glands with fibrous stroma showed thick wall blood vessels (H&E, x100). D) Endometrial hyperplasia with varying sized hyperplastic glands, many of which are large and cystically dilated and are lined by hyperplastic epithelium (H&E, x100). E) Endometrial adenocarcinoma showing increase in the number of glands which are closely packed sometimes showing ‘back-to-back crowding’ due to obliterated intervening stroma. The glandular epithelium shows stratification, formation of tufting and papillae and atypical changes (H&E, x100).

Overall, in the reproductive age group, the most common histological finding was the normal menstrual pattern (27/54 cases, 50%) (Figure 3).

Whereas, in the perimenopausal age group, the most common histological finding was simple endometrial hyperplasia (19/97 cases, 19.6%), followed by disordered proliferative endometrium (16/97 cases, 16.5%) (Figure 4).

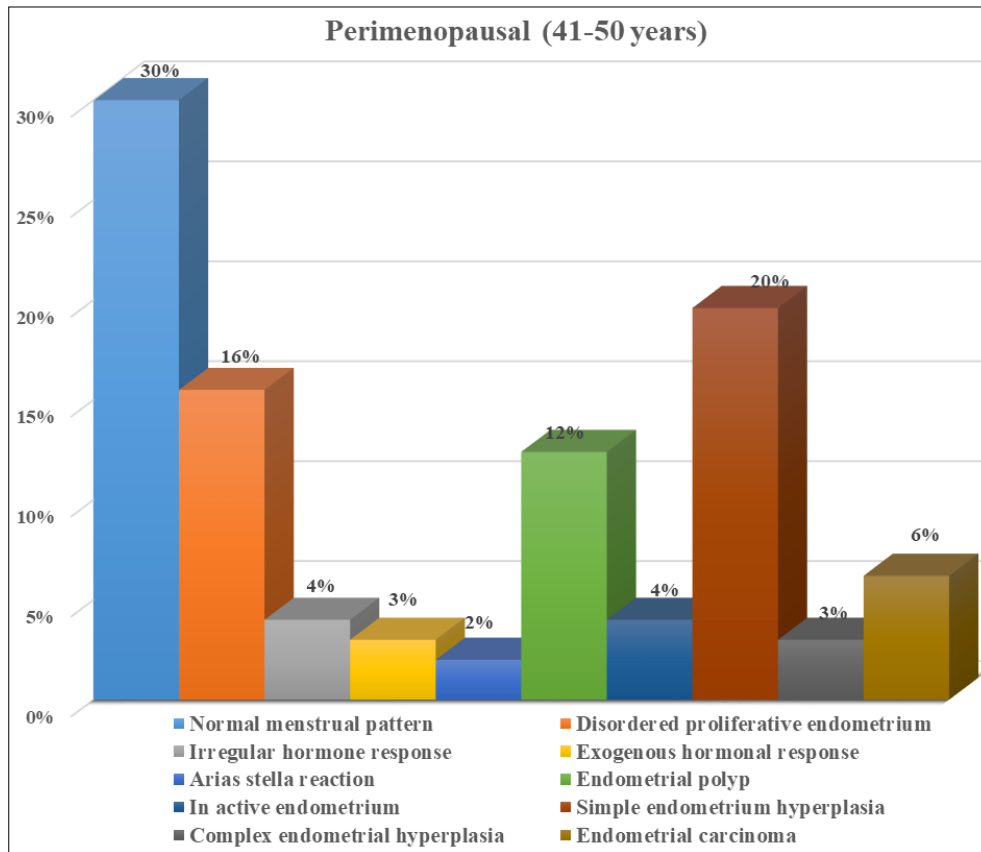
In the postmenopausal age group, the most common histological finding was endometrial polyp (24/79 cases, 30.4%) followed by simple endometrial hyperplasia (17/79 cases, 62.5%), inactive endometrium (8/79 cases, 10%), and endometrial carcinoma (8/79 cases, 10%) (Figure 5).



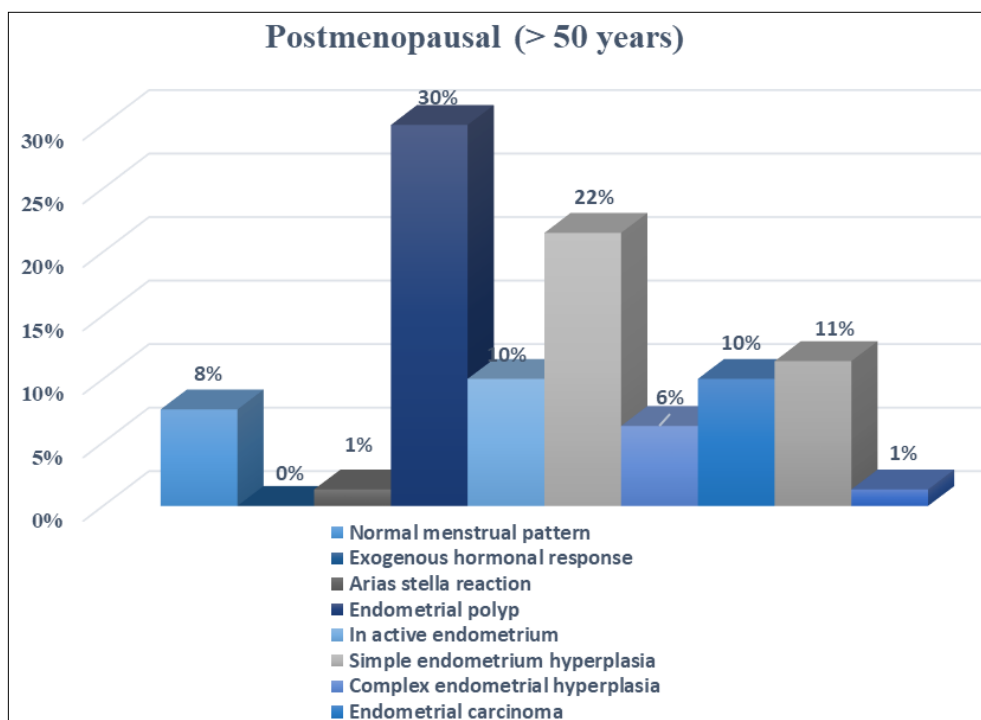
**Fig 3: Different histological pattern in reproductive age group.**

The most common pattern was normal menstrual pattern followed by disordered proliferative endometrium. No cases

of inactive endometrium or complex endometrial hyperplasia were reported in this age group.



**Fig 4:** Different histological pattern in perimenopausal age group. The most common pattern was normal menstrual pattern followed by simple endometrial hyperplasia, disordered proliferative endometrium and endometrial polyp.



**Fig 5:** Different histological pattern in postmenopausal age group. The most common pattern is endometrial polyp followed simple endometrial hyperplasia.

**Discussion**

AUB is an abnormal uterine bleeding which needs medical intervention in almost all cases, as it can lead to anemia and morbidity in women [8]. AUB is either caused by hormonal disturbance called as dysfunctional uterine bleeding or organic diseases such as polyps, hyperplasia and

malignancy [7, 8]. In this study, based on age, the patients have been divided into 3 groups, the reproductive age group (20-40 years), the perimenopausal age group (41-50 years) and the postmenopausal age group (> 50 years). The large number of cases presented with AUB, in this study was seen in perimenopausal age group, the same finding was reported

in a previous study<sup>[9]</sup>. The results presented here indicate that, majority of the cases of normal physiological changes (50%), either the proliferative or the secretory phases of endometrium, were under 40 years of age, this result correlated with other studies done previously<sup>[10, 11, 12, 13]</sup>. A large number of normal mensural pattern was also seen in perimenopause group<sup>[14]</sup>. Exogenous hormonal therapy, especially the ones that contain both estrogen and progesterone result in a weak or poorly developed secretory endometrium<sup>[15, 16]</sup>. In the present study, few cases, in all groups, showed endometrial changes due to exogenous hormones. Other hormonal changes such as Arias-Stella reaction and irregular hormonal response were also detected in this work as well as in other study<sup>[7]</sup>. Endometrial polyps were the commonest finding in postmenopausal group in about 30% of the case. With diminished prevalence of cases in perimenopausal and reproductive age group, 12% and 4% respectively. This is inconsistent with report by Kim et al<sup>[17]</sup> which revealed a high frequency of endometrial polyp in perimenopausal women. Disordered proliferative endometrium is a histological feature similar to simple hyperplasia, but the process is more suggestive of focal than diffuse. Disordered proliferative endometrium is also defined as an exaggeration of the normal proliferative phase without significant increase in the overall ratio of glands to stroma<sup>[18]</sup>. In our study, it was seen in 20% of reproductive women and in 16% in perimenopausal cases, with few numbers in postmenopausal patients with same result seen in previous research<sup>[19]</sup>. Endometrial hyperplasia is classified according to the 1994 World Health Organization (WHO) scheme into simple and complex hyperplasia<sup>[20]</sup>. Simple endometrial hyperplasia was the most common cause of uterine bleeding in postmenopausal and perimenopausal women with percentage of 22% and 20% respectively whereas complex hyperplasia only seen in 6% and 3% of post and perimenopausal women respectively, very few cases were detected in reproductive patients. Our findings are in agreement with previous studies<sup>[21]</sup>. Regrading malignancy, our data revealed that the incidence of endometrial carcinoma was 10%, 6% and 4% in post, perimenopausal and reproductive age group respectively. A different result was recorded by Dangal G in 2003 where the incidence of endometrial cancer in the postmenopausal group was 17.6%<sup>[22]</sup>. However, Dhakal *et al.*, also observed a low incidence of endometrial cancer with only 2% of all gynecological cancers with the mean age of 56.7 years<sup>[23]</sup>. This study has shown that the most common histopathological pattern of cancer cases were endometrial carcinoma, no other histological subtypes were recorded. In general, most of endometrial malignancy were detected in postmenopausal women (above 55 years) and the high or low incidence of this type of cancer of cases in different studies is related to the population of the study and environmental causes<sup>[24]</sup>.

### Conclusions

This study showed that large number of patients with AUB, in reproductive age group, showed either normal physiological changes or slight disturbed menstrual pattern such as in disordered proliferative endometrium. In perimenopausal age group, AUB was either associated with normal physiological changes or due to simple endometrial hyperplasia. Whereas endometrial polyp was the most common pathology causing AUB in postmenopausal

women. In general, all age groups showed low incidence of gynecological malignancy. In general, postmenopausal age group with AUB, carry the higher risk of malignancy.

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