Original paper

The Frequency of Histopathological Patterns in Endometriam Obtained from a Sample of Iraqi Women with Abnormal Uterine Bleeding

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Abstract

Background: Abnormal uterine bleeding is one of the most common and challenging problems to the gynecologist regardless of the age of the women. Histopathological evaluation of endometrium regarded as an important step in the diagnosis and management of endometrial causes of Abnormal Uterine Bleeding.

Objective: To study the frequency of different histopathological patterns of endometrium in women with abnormal uterine bleeding across different age groups.

Materials and methods: A retrospective age specific comparative analysis was done using a total number of women (85) presenting with abnormal uterine bleeding who underwent endometrial sampling during one year period from January 2015 to march 2016 in the pathology department of AL elwia teaching hospital. Endometrial curettages done for evaluation of products of conception were excluded. Endometrial samples were sent for histopathological examinations and different histological patterns were noted.

Results: Abnormal uterine bleeding was found to be more frequent in women in age 41 to 60 years and less frequent in the age over 60 years. The most common histopathological feature present in the curetting materials of women with abnormal uterine bleeding was inadequate proliferative endometrium (which belong to inorganic cause of AUB*dysfunctional*) in both age group 20 to 40 years and 41 to 60 years, and represent (44.7%) of total samples, while none of the samples in women over 60 years showed inadequate proliferative endometrium. Endometrial carcinoma was diagnosed in five samples, representing (5.88%) of all samples, all were of grade I endometriod type and all were in the age group 41 to 60 years which represent (8.62%) of all the samples in this age group. Only one sample (1.17%) showed malignant mixed Mullerian tumor. Regarding endometrial hyperplasia, 14 were simple hyperplasia without atypia representing 16.47% of all samples, all were without atypia, while only one sample (1.17%) showed complex atypical hyperplasia .This study also showed that 15 samples (17.64%) were due to endometrial polyps. Two samples (2.35%) showed irregular secretory endometrium. Three samples (3.52%) showed histological evidence of exogenous hormone administration, while six samples (7%) were not conclusive.

Conclusions: Abnormal uterine bleeding in women below 60 years old is most commonly dysfunctional in origin. In addition, a good number showed underlying organic pathology, thus highlighting the importance of endometrial curettage and biopsy as a diagnostic procedure in the evaluation of women (particularly over 40 years old) with abnormal uterine bleeding for an early detection of ominous lesions such as endometrial adenocarcinoma and its precursors since histopathological findings of endometrium regarded as the main basis of management desescin

Keywords: Abnormal Uterine bleeding, Endometrium, hyperplasia.

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Introduction

Abnormal uterine bleeding (AUB) is a common complaint in all gynecological departments, which is defined as Bleeding that differs in amount or timing from a woman's usual menstrual flow [(1)]. Endometrial sampling for histological examination done by the gynecologist is an important step in the evaluation of women with abnormal uterine bleeding, but a relevant clinical history, including age, menstrual history and menopausal status, and knowledge on the use of exogenous hormones and tamoxifen, is mandatory for pathologists to accurately evaluate any endometrial biopsy, otherwise the underlying cause of dysfunctional uterine bleeding cannot be detected [(2)]. Both benign and malignant causes could be found during evaluation of women with AUB ,one of benign cause frequently seen in endometrial sampling is endometrial polyp, which is identified histologically as benign glandular proliferation set in a stroma containing thick wall blood vessels[(3)]. To date, endometrial biopsy are not used for dating the endometrium and assessing whether ovulation has occurred or not, because biochemical analysis of various hormones give equivalent or better information[(4)] .Some pathologists report that (the Specimens are Insufficient for diagnosis) Because some gynecologists are less aggressive in obtaining samples and may not yield adequate tissue.[(5)]

The most frightening cause of abnormal uterine bleeding is endometrial carcinoma[(2)] .The most common type of endometrial carcinoma is endometrioid type which is estrogen-dependent and frequently associated with endometrial hyperplasia, the nomenclature of these hyperplasia is an important histopathological task., because The highest risk for metachronous carcinoma is associated with atypical hyperplasia of the endometrium as detected in the curetting materials [(5,6)] .Endometrial Hyperplasia is classified in to simple hyperplasia and complex hyperplasia, both are subdivided into with or without atypia according to the criticisms of the kurman-norris scheme, which is regarded as the recent classification scheme and no other classification system is ready to replace it at present[(7)]

Endometrial hyperplasia usually detected following investigation of females with symptoms of abnormal uterine bleeding [(8)] and histological examinations regarded as the gold slandered for diagnosis. [(9)] Simple (cystic) hyperplasia, identified histologically "by minimal endometrial glandular crowding and with low risk of progression to endometrial carcinoma, while complex hyperplasia, characterized by greater endometrial glandular crowding and intermediate risk of progression and atypical hyperplasia, comprised of endometrium with complex glandular crowding and/or cytological atypia and the greatest risk of endometrial carcinoma progression".[(9,10)]

Cystic or simple hyperplasia will progress to cancer in less than 5 percent of patients, therefore most women with simple hyperplasia without any atypia can be treated in a conservative way, while atypical complex hyperplasia is a premalignant lesion that progresses to cancer in 30 to 45 percent of women[(5)]. Most gynecologists needed another sample to exclude the presence of endometrial carcinoma because hysterectomy is the treatment choice for complex or high-grade hyperplasia and endometrial adenocarcinoma[(11)]. Regarding the latter, tumor grade and histological subtype are made according to certain histological criteria. (Nuclear features and the proportion of solid tumor vs. identifiable glands defines grade 1–3), while Histological subtype is decided by morphologic features and often aided by immunohistochemical markers [(12)]. Endometrial cancers are classified into 2 broad histological types, defined as type I and type II. Type I consists of

endometriosis carcinoma and its histological variants; type II endometrial cancer includes serous carcinoma, clear cell carcinoma, and carcinosarcoma [13]. Endometrioid tumors often have a favorable prognosis and typically present at an early stage, while other histological types of endometrial carcinoma (eg, serous, clear cell) as well as other types of uterine cancer carry a poor prognosis [14]. Sometime morphological distinction between a case of complex atypical hyperplasia and well differentiated adenocarcinoma can be difficult, largely because of the fact that endometrial hyperplasia and carcinoma represent two points in the same pathological continuum at the morphological, ultrastructural, immunohistochemical and molecular levels[7], however some helpful histological features if present in a biopsy specimen favor the diagnosis of endometrial carcinoma over complex atypical hyperplasia include the absence of stromal background, confluent glandular pattern with cribriform and intraglandular bridging, extensive papillary formation[2].

Materials and Methods

This is a retrospective age specific study including all endometrial sampling materials received for histopathological evaluation of abnormal uterine bleeding in the Histopathology Department, of al Elwia Hospital, one of specialized teaching hospital for obstetrics and gynecology in Bagdad during one year, in the period between January 2015 and March 2016 were included in this retrospective study. Endometrial curettages done for evaluation of products of conception were excluded. The clinical information regarding age, hormone therapy and intrauterine contraceptive device (IUCD) usage were retrieved from the biopsy request forms. Because it's a retrospective study, so other clinical informations were missed. The patient's age ranged from 20 to 69 years, subdivided into three age groups.

Microscopic reevaluation and the patterns of histopathological changes were identified and classified into nine diagnostic categories according to certain histological criteria listed in (rosai and Akerman surgical pathology) including the resent classification scheme of endometrial hyperplasia stated by kurman-norris [7,15] as shown figures 2-7.

After microscopic reevaluation of histopathological slides that were retrieved, diagnostic concordance was 97% (83 out of 85 samples had the same diagnosis as listed in the biopsy results recorded in patient's archive). Only two samples recorded as simple hyperplasia without atypia after reevaluation diagnosed as fragmented endometrial polyps.

Results

The study enrolled 85 cases of women with abnormal uterine bleeding (AUB).The ages of the women ranged from 20 to 69 years with a mean age 44.23 ± 9.55 years. The histopathological diagnosis is listed in Table 2

They were subdivided into three age groups 23(27%) were in the age group 20 to 40 years, 58(68.23%) in the age group 41 to 60 years, 4(4.7%) above 60 years old. Abnormal uterine bleeding were found to be more frequent in women age 41 to 60 years and less frequent in the age over 60 years in which only four samples were obtained. Table 3. Figure 1

The most common histopathological feature present in the curetting materials of women with abnormal uterine bleeding was Inadequate proliferative endometrium which in both age group 20 to 40 years and 41 to 60 years, and represent (44.7%) of all the samples, while none of the samples in the women above 60 years showed proliferative endometrium. Endometrial carcinoma was found in five samples, (5.88%) of all the samples ,all were of

grade I endometriod type according to FIGO grading system[7] and all were in the age group 41 to 60 years, which represent (8.62%) of all samples in this group. Only one sample (1.17%) showed malignant mixed Mullerian tumor. Regarding endometrial hyperplasia, simple hyperplasia represent 16.47% of all the samples, all were without atypia, while only one sample (1.17%) showed complex atypical hyperplasia.

Table 1. Histological criteria used for selection of samples (7, 15)

Diagnostic category	Microscopic picture
Simple hyperplasia without atypia	Proliferation of cystically dilated endometrial glands lined by cells without atypia
Atypical complex hyperplasia	Proliferation of complex irregular endometrial glands lined by cells with obvious atypia without stromal invasion
Endometrial adenocarcinoma	Presence of irregular complex branching glands lined by cells with obvious atypia with loss of polarity , cribriform and intraglandular bridging extensive papillary formation stromal invasion
Malignant mixed mullerian tumor	Both glandular and stromal component are malignant[7]
Endometrial polyp	Benign glandular proliferation, thick wall blood vessels
Inadequate Proliferative endometrium*	Benign endometrial glands in proliferative phase of menstrual cycle
Irreguler Secretory endometrium	Underdeveloped secretory endometrium or secretory and proliferative endometrium in same specimen
Exogenous hormone(progestin) **	Atrophic or weak secretary endometrial glands set in an expanded stroma with pseudodecedualization
Not conclusive	Small amount of tissue with few or no glands making the diagnostic decision is difficult

* Inadequate Proliferative endometrium usually diagnosed when there is a disparity between clinical menstrual cycle date and microscopic changes2

**In this study all samples belong to women who were on progestin medication to control dysfunctional uterine bleeding

Table 2. Histopathological diagnosis of 85 samples from women with AUB

Histopathological diagnosis	Total number	Percentage
Inadequate proliferative endometrium	38	44.7 %
Endometrial polyp	15	17.64 %
Simple cystic hyperplasia	14	16.47 %
not conclusive	6	7 %
Endometrial adenocarcinoma	5	5.88 %
Exogenous hormone	3	3.52 %
Irreguler Secretory endometrium	2	2.35 %
Complex atypical hyperplasia	1	1.17 %
Malignant mixed mullerian tumor	1	1.17 %
Total numbers	85	100 %

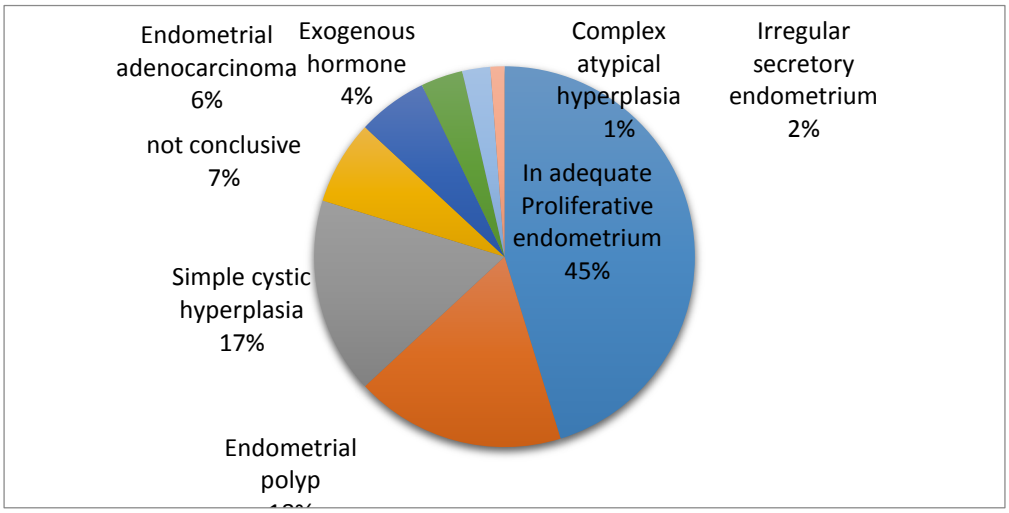


Figure 1. Histopathological diagnosis of 85 samples from women with AUB

Table 3. Distribution of histopathological diagnosis in different age groups

Histopathological diagnosis	20 40 years	41 60 years	Above 60 years	Total number	Percentage
Simple cystic hyperplasia	2	11	1	14	16.47 %
Complex hyperplasia	0	0	1	1	1.17 %
Endometrial adenocarcinoma	0	5	0	5	5.88 %
Malignant mixed mullerian tumor	0	0	1	1	1.17 %
Endometrial polyp	7	7	1	15	17.64 %
Inadequate proliferative endometrium	9	29	0	38	44.7 %
Irreguler Secretory endometrium	1	1	0	2	2.35 %
Exogenous hormone	2	1	0	3	3.52 %
not conclusive	2	4	0	6	7 %
Total numbers	23	58	4	85	100 %

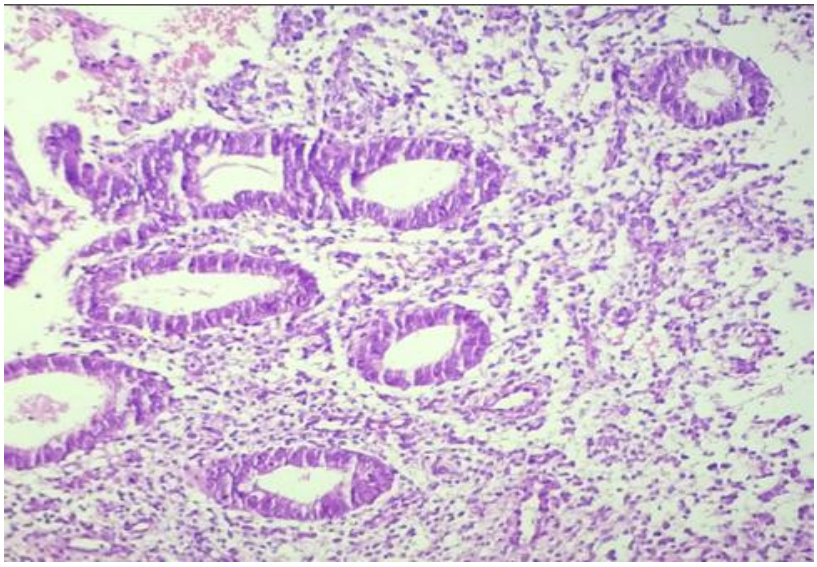


Figure 2: (x100) H&E stained slide demonstrate histology of simple endometrial hyperplasia without atypia

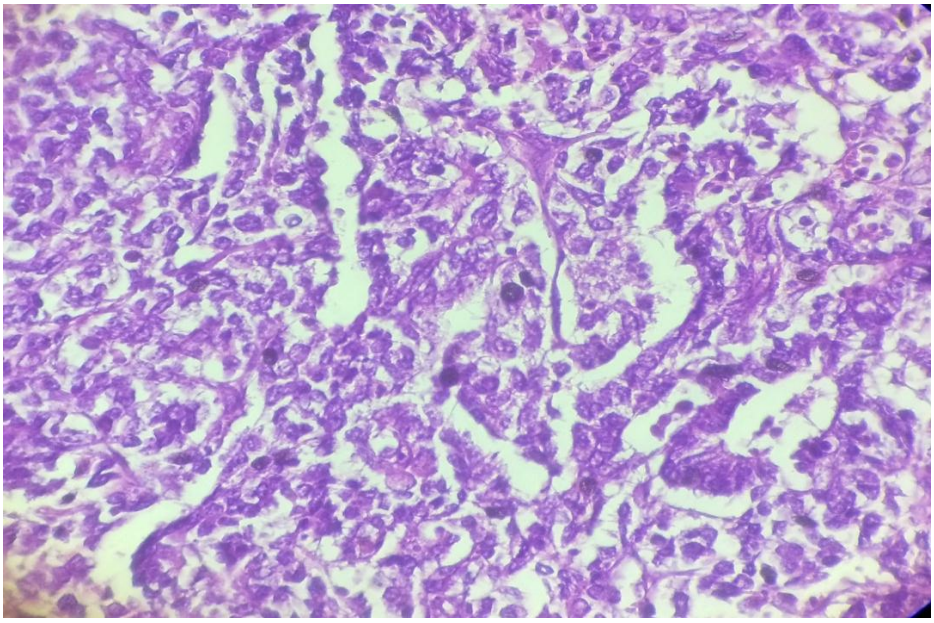


Figure 3: (x100) H&E stained slide demonstrate histology of malignant mixed mullerian tumor

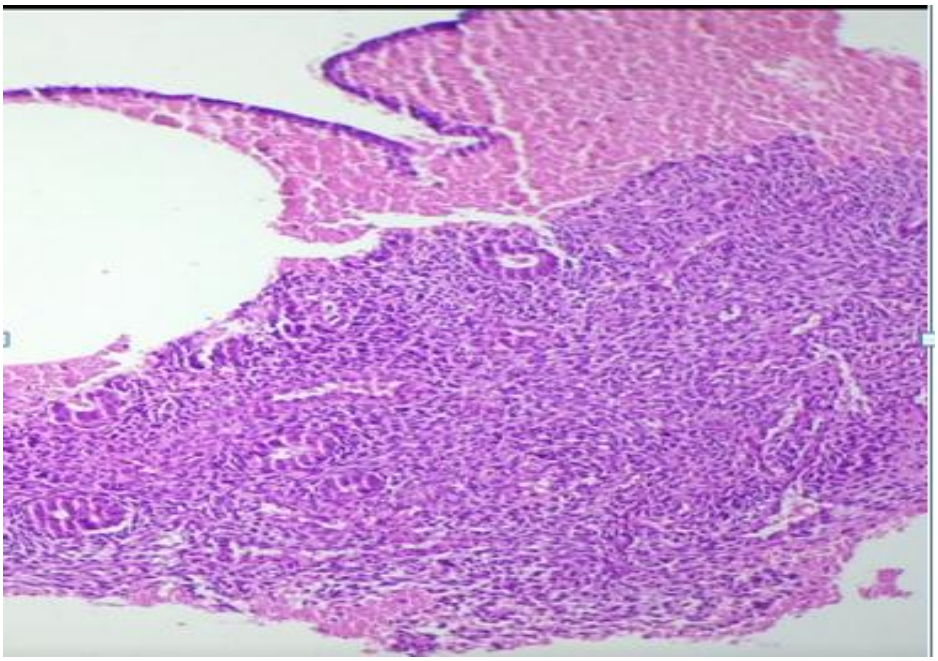


Figure 4:(X100) H&E stained slide demonstrate histology of benign endometrial polyp

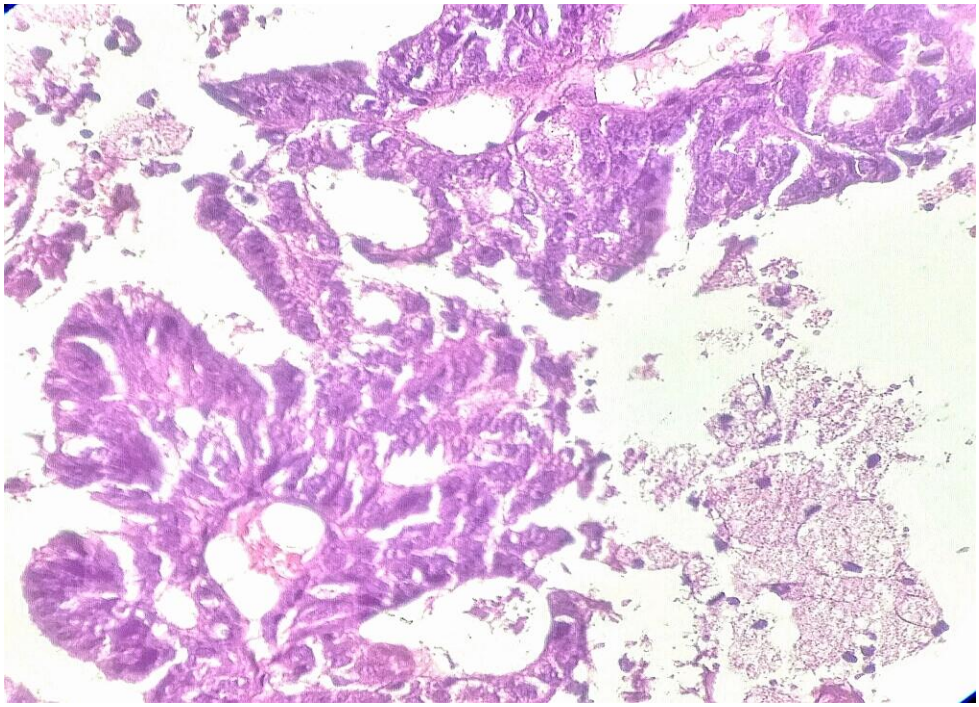


Figure 5: (x100) H&E stained slide demonstrate histology of endometrial adenocarcinoma

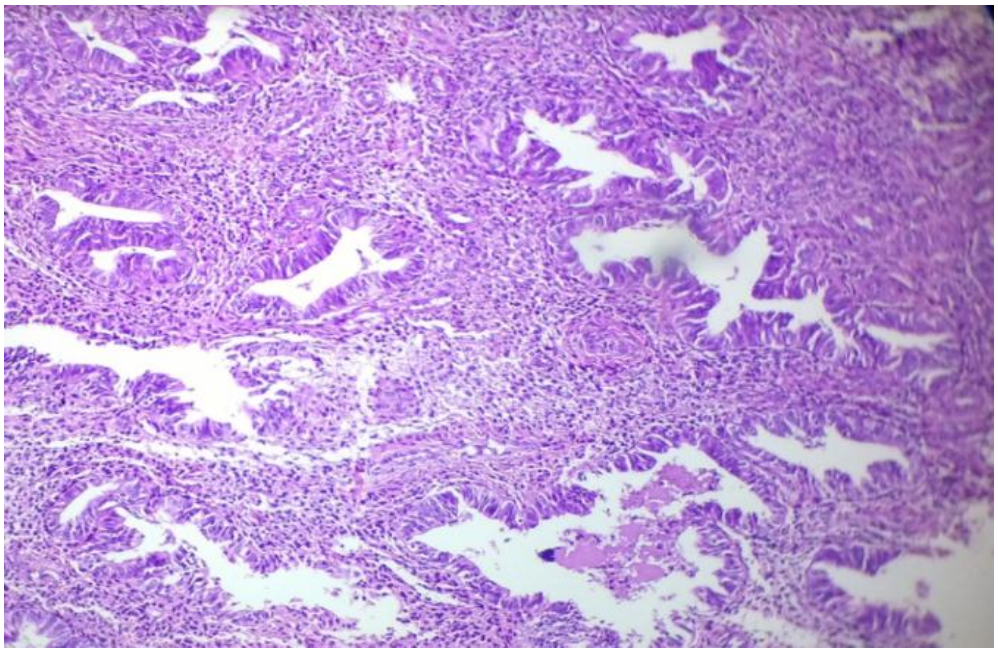


Figure 6 A

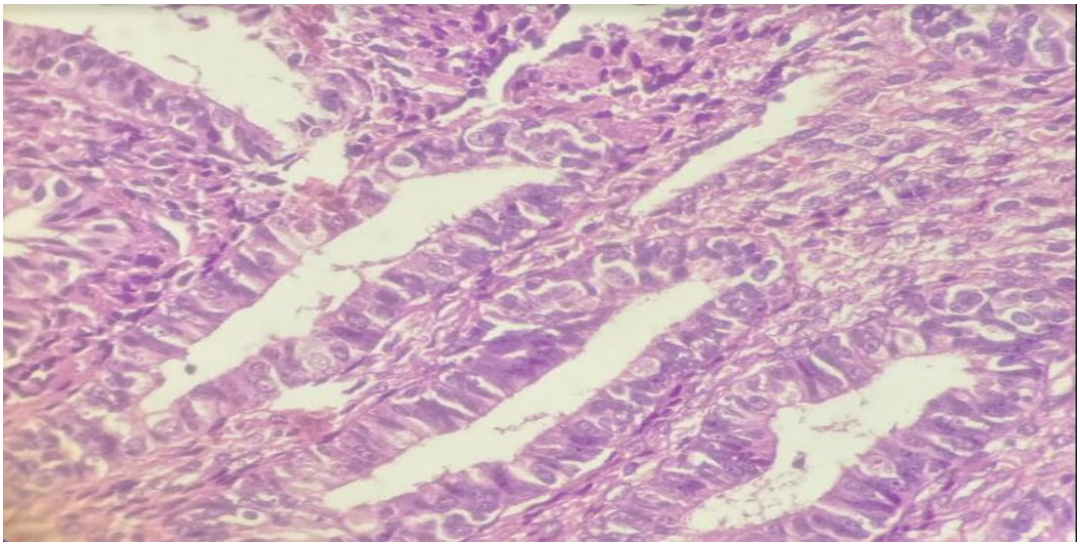
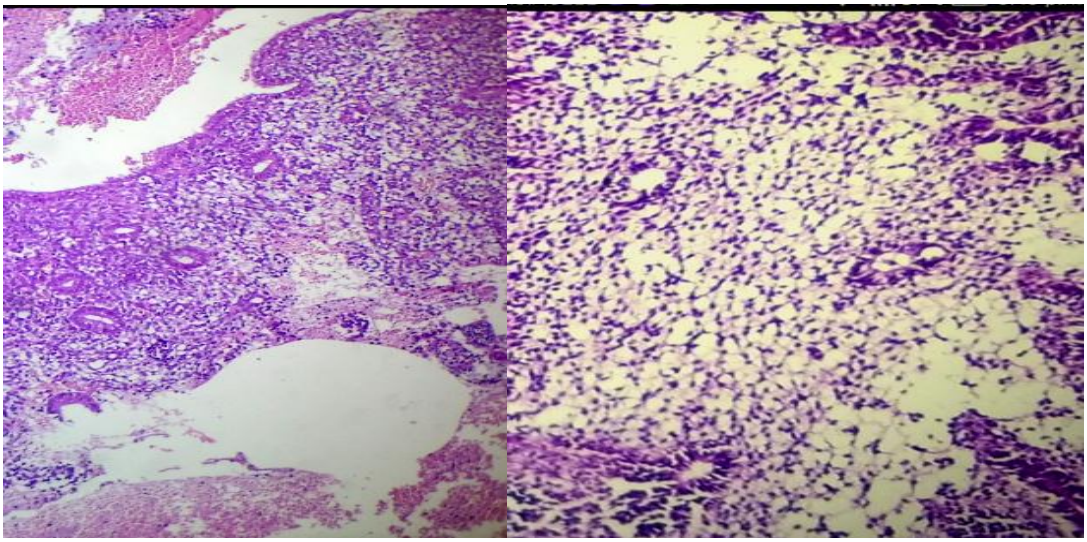


Figure 6 B

Figure 6 (A&B). H&E stained slide demonstrate histology complex atypical hyperplasia (A:X100, B:X400)



A **B**

Figure 7(A&B)

Figure 7A:(X100) histology of inadequate proliferative endomtrium

Figure 7B:(X100) histology of irreguler secretory endometrium

This study also showed that 15 samples (17.64%) showed endometrial polyps. Two samples (2.35%) showed irregular secretary endometrium. Three samples (3.52%) showed histological evidence of exogenous hormone administration, those samples were for women below 60 years which already have a clinical note that they were on progestin treatment (to control dysfunctional uterine bleeding) in their biopsy request forms, while six samples (7%) were none conclusive. Regarding women 20 to 40 years old, inadequate proliferative endometrium were

the most common pathology responsible for abnormal uterine bleeding, then endometrial polyps, then simple cystic hyperplasia and exogenous hormone, and only one sample was Irregular secretory endometrium.

Regarding women 41 to 60 years old ,inadequate proliferative endometrium were the most common pathology then simple cystic hyperplasia then endometrial polyps then adenocarcinoma and only one sample was Irregular secretory endometrium .

Regarding women above 60 years old, there were only four samples, one simple cystic hyperplasia, one complex atypical hyperplasia, one malignant mixed mullerian tumor and one endometrial polyp.

Discussion

Abnormal uterine bleeding can occur due to structural causes in the uterus or due to functional causes related to ovulation [(1)]. Endometrial curettage is a routine diagnostic procedure in the evaluation of menstrual disorders [(2)]. This study showed abnormal uterine bleeding was more frequent in women 41 to 60 years and less frequent in the age over 60 years, this results agree with one Iraqi study done by Nadia etal[16] and two other Indian studies (Alpana etal and Safia etal)[(17, 18)]. The most common histopathological features present in women with abnormal uterine bleeding in this study were inadequate proliferative endometrium (44.7%). Proliferative endometrium considered normal if it's found in the first half of the cycle and indicative of anovulation if it is found in the second half[1]. The results agree with the data published by Nadia etal and Alpana etal [(16,17)] and disagree with the data published by Safia etal and Spencer etal [(18,19)] in which they found irregular secretory endometrium was the most common cause, but all these studies in addition to this study consider functional causes accounted for the majority of the diagnosis of abnormal uterine bleeding and the resulting bleeding called dysfunctional uterine bleed (DUB) [(16)]

Endometrial carcinoma were found to be in 5.88% of all the samples this results are higher than the results in the studies done by Nadia etal and Alpana etal [(16,17)] in which their results were 2%, 1% respectively. These variation may indicate a recent increase in the incidence of endometrial carcinoma over the last years and should be taken seriously. This study showed all the five cases of endometrial carcinoma were low grade endometriod type, while Alpana etal [(17)] showed types other than endometriod, largely attributed to variation in sample size. Endometrial adenocacinoma in this study were more common in women 41 to 60 years old, which represent (8.62 %) of samples in this age group .This results agree with the results of Alpana etal [(17)]

Malignant mixed mullerian tumor represent (1.17 %) ,only one case in 65 years old woman with post-menopausal bleeding, its diagnosed when both epithelial and stromal components of the tumors is malignant [(7)], its a rare tumor and unusually diagnosed in endometrial curetting specimen. Simple cystic hyperplasia represent 16.47% of the samples, all were without atypia while only one sample (1.17%) showed complex atypical hyperplasia, this results agree with results obtained by Alpana etal [(17)]

This study showed (44.7%) of all the samples were inadequate proliferative endometrium. The result is higher than in a study done by Safia etal [(18)] which showed the percentage was (37 %). Irregular secretory endometrium represent (2.35%) of all samples due to, luteal phase defect, which is characterized by an insufficient production of progesterone by the corpus luteum and, therefore, an inadequate development of the secretory endometrium [(1)], nearly similar results found in a study done by Safia etal[(18).] Endometrial polyp present in (17.64%) of all the samples, polyps at times are difficult to re recognize

in curettage specimens, they were identified as polypoidal fragments with epithelium on three sides[2]. Another identifying feature was the presence of fibrous stroma and thick walled blood vessels that had a contrasting appearance to the other endometrial fragments [(7)]. Nadia etal and Safia etal [(16,18)] showed the frequency of endometrial polyps were13.8%, 2.7% respectively due to variation in sample size

In this study only three samples showed the pathological evidence of exogenous hormone administration (progestin) which represent (3.52%) of all samples (those samples were for women below 60 years which already have a clinical note in their biopsy request forms that they were on progestin treatment (to control dysfunctional uterine bleeding) which was compatible with histological features) , this results agree with one study done by Safia etal [(18)]. When endometrial biopsy showed unusual, non-cyclical appearance of the endometrium, the pathologist should ask women about the usage of exogenous hormones[4]. Some hormone preparations, especially those with both estrogen and progestogen (most modern hormone replacement therapy), usually give a morphological features of weak or poorly developed secretory type endometrium, whereas other preparations result in atrophic endometrium.[(2)] The endometrial curetting's were scanty and regarded as inadequate for diagnosis in 0.04%, Nadia etal and Safia etal [(16,18)] showed somewhat a higher percentage which is due to the effect of personal efficiency in obtaining the curetting materials.

Regarding women 20 to 40 years old, inadequate proliferative endometrium were the most common pathology, this results agree with results of Khare A etal [20,] then endometrial polyp, then simple cystic hyperplasia and exogenous hormone, and only one case was irregular secretory endometrium. Regarding women 41 to 60 years old, inadequate proliferative endometrium were the most common pathology, this results agree with the results of **.** Khare A etal[20], then simple cystic hyperplasia, then endometrial polyps, then adenocarcinoma, and only one case was irregular secretory endometrium.

Conclusions

Abnormal uterine bleeding in women below 60 years old is most commonly dysfunctional in origin. However a good number showed underlying organic pathology, highlighting the importance of endometrial curettage and biopsy as a diagnostic procedure in the evaluation of women (especially those above 40 years old) with abnormal uterine bleeding for an early detection of ominous lesions such as endometrial adenocarcinoma and its precursors since histopathological findings of endometrium regarded as the main basis of management desescin

Recommendations

A prospective study on abnormal uterine bleeding should be done with a good cooperation between both the gynecologists and the pathologists to overcome the missing of the relevant clinical information usually seen in each retrospective study like the clinical type of AUB (menorhagia, metrorhoragia..etc), parity, menstrual history ,marital status, and any associated medical problems and to achieve a better follow-up of cases that managed conservatively.

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