Histopathological pattern of abnormal uterine bleeding in endometrial biopsies

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ABSTRACT

Abnormal uterine bleeding is a common presenting complaint in gyanecology out patient department. Histopathological evaluation of the endometrial samples plays a significant role in the diagnosis of abnormal uterine bleeding. This study was carried out to determine the histopathological pattern of the endometrium in women of various age groups presenting with abnormal uterine bleeding. Endometrial biopsies and curettings of patients presenting with abnormal uterine bleeding was retrospectively studied. A total of 403 endometrial biopsies and curettings were analyzed. The age of the patients ranged from 18 to 70 years. Normal cyclical endometrium was seen in 165 (40.94%) cases, followed by 54 (13.40%) cases of disordered proliferative endometrium and 44 (10.92%) cases of hyperplasia. Malignancy was seen in 10 (2.48%) cases. Hyperplasia and malignancy were more common in the perimenopausal and postmenopausal age groups. Histopathological examination of endometrial biopsies and curettings in patients presenting with abnormal uterine bleeding showed a wide spectrum of changes ranging from normal endometrium to malignancy. Endometrial evaluation is specially recommended in women of perimenopausal and postmenopausal age groups presenting with AUB, to rule out a possibility of any preneoplastic condition or malignancy.

Keywords: Abnormal uterine bleeding, carcinoma, endometrium, hyperplasia.

INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle or after menopause.[1]

It is considered one of the most common and challenging problems presenting to the gynaecologist and is responsible for as many as one-third of all outpatient gynaecologic visits.[2,3] AUB can be caused by a variety of systemic diseases such as endocrine disorders or drugs. On the other hand, it may be related to pregnancy, anovulation, fibroids, polyps, adenomyosis or neoplasia.[4]

The importance of endometrial biopsy or curettage done to obtain material for histopathological evaluation, to aid in diagnosis and further management, cannot be overemphasized especially in perimenopausal females who are at a risk of developing malignancy.[5]

This study was carried out to determine the histopathological pattern of the endometrium in women of various age groups presenting with abnormal uterine bleeding.

MATERIALS AND METHODS

This study was conducted at the Department of Pathology, Patan Academy of Health Sciences (PAHS), Lalitpur, Nepal. A total of 403 patients presenting with abnormal uterine bleeding over a period of 2 years from April 2011 to March 2013 were included in the study.

The histopathological findings of AUB were categorized into functional and organic causes. The functional causes of AUB included in this study were normal cyclical phases (proliferative and secretory) of the endometrium and other abnormal physiological changes in the endometrium (atrophic endometrium, weakly proliferative endometrium, disordered proliferative endometrium and pill endometrium). Organic intrauterine lesions which were the cause of AUB in this study include chronic endometritis, hyperplasia, polyp and endometrial carcinoma.

Patients were also categorized into the following age groups: reproductive (18-40 years), perimenopausal (41-50 years) and postmenopausal (> 50 years). Patients with bleeding due to cervical pathology, pregnancy related complications such as abortions, gestational trophoblastic diseases or ectopic pregnancy were excluded from the study.

Endometrial specimens were obtained by either endometrial biopsy or curetting and fixed in 10% formalin. The specimens were processed routinely and stained with Haematoxylin and Eosin (H&E) stain. Data was analyzed using the Statistical Package for Social Science (SPSS version 17) for windows.

RESULTS

A total of 403 endometrial biopsies and curettings from patients with abnormal uterine bleeding (AUB) were analyzed. The cause of AUB could be determined in only 379 out of 403 endometrial biopsies as 24 biopsy specimens were inadequate for evaluation. Of the remaining 379 cases, 307 (81%) were due to functional causes as no organic pathology was found, while the remaining 72 cases (19%) showed definite endometrial pathology (Table-1).

Table-1: Distribution of cases of AUB according to cause

Cause of AUB	Total	%
Functional causes	307	81
Organic lesions	72	19
Total	379	100

Out of the 307 functional cases of AUB, secretory endometrium and proliferative endometrium were the most common patterns and were seen in 91 cases (29.64%) and 74 (24.10%) cases, respectively. This was followed by 54 (17.59%) cases of disordered proliferative endometrium (17.59%).

Amongst the 72 organic lesions causing AUB, endometrial hyperplasia was the most common and seen in 44 (61.11%) cases. Simple hyperplasia without atypia was the most common type of hyperplasia and was observed in 30 (97.44%) patients. The other organic causes of AUB observed in this study include 25 (34.72%) cases of pill endometrium, 13 (18.06%) cases of chronic endometritis and 10 (13.89%) cases of malignancy.

The age of the patients presenting with AUB ranged from 18 to 70 years with a mean age of 43 years. A total of 186 (46.15%) patients presenting with AUB were seen in the perimenopausal age group, followed by 154 (37.97%) patients in the reproductive age group (Table-2).

Table-2: Age group of patients presenting with AUB

Age group (years)	Total	%
18 - 40 years (reproductive)	153	37.97
41- 50 years (perimenopausal)	186	46.15
> 50 years (postmenopausal)	64	15.88
Total	403	100

Histopathological examination of the endometrium showed various histological patterns in AUB (Table 3). Patterns of normal cyclical endometrium (proliferative and secretory phases) were the most common and seen in 165 (40.94 %) cases presenting with AUB. They were also the predominant patterns seen in all the three age groups.

Disordered proliferative endometrium and hyperplasia were the next common histological patterns which were seen in 54 (13.40%) and 44 (10.92%) cases, respectively. Both these patterns were commonly seen in the perimenopausal age group. Out of the 44 cases of hyperplasia, there were 30 (68.18%) cases of simple hyperplasia without atypia and 7 (15.91%) cases of complex hyperplasia without atypia.

Weakly proliferative endometrium and pill endometrium wee seen in 39 (9.68%) and 25 (6.2%) cases, respectively. Both these patterns were commonly seen in the 18-40 and 41-50 age groups. Atrophic endometrium comprised of 19 (4.71%) cases which was seen in both the perimenopausal and postmenopausal age groups. Malignancy was a cause of AUB in only 10 (2.48%) cases, 6 (60%) of which were diagnosed after menopause (Table-3).

Table-3: Histopathological patterns according to age group

Histopathological diagnosis	Age group (years)			Total	%
	18-40	41-50	> 50		
Proliferative	29	35	10	74	18.36
Secretory	41	37	113	91	22.58
Atrophic	-	8	11	19	4.71
Weakly proliferative	18	21	-	39	9.68
Disordered proliferative	22	28	4	54	13.40
Deficient luteal phase	3	2	-	5	1.24
Chronic endometritis	4	7	2	13	3.23
Endometrial polyp	1	2	2	5	1.24
Simple hyperplasia without atypia	9	16	5	30	7.44
Simple hyperplasia with atypia	1	3	1	5	1.24
Complex hyperplasia without atypia	2	3	2	7	1.74
Complex hyperplasia with atypia	-	1	1	2	0.50
Pill endometrium	15	10	-	25	6.20
Endometrial carcinoma	1	3	6	10	2.48
Unsatisfactory for evaluation	7	10	7	24	5.96
Total	153	186	64	403	100

DISCUSSION

Abnormal uterine bleeding is a commonly encountered gynaecological problem.[6] It includes both dysfunctional uterine bleeding (DUB) and bleeding from structural causes like fibroids, polyps, endometrial carcinoma and pregnancy complications.[7] Dysfunctional uterine bleeding is defined as abnormal uterine bleeding without a demonstrable organic cause.[8] In most instances dysfunctional uterine bleeding is due to the occurrence of an anovulatory cycle.[9] It can be diagnosed after exclusion of structural, iatrogenic, medications, pshycological and systemic disorders by various diagnostic techniques.[10]

In about 25% of the patients, the abnormal bleeding is the result of a well defined organic abnormality.[11] Organic cause of AUB was determined in 72 (19%) cases in this study which is consistent with data published by Ara et al. (21.73%) and Moghal (22.5%).[12,13] (15-3). Endometrial hyperplasia was the most common organic cause of AUB which was seen in 44 (61.11%) cases. Similar data (62.8%) was published by Anwer *et al*.[14]

Abnormal and excessive endometrial bleeding occurs in reproductive women of all age groups but is more common in adolescent and perimenopausal women.[15] Many studies have revealed that occurrence of menstrual disorders increases with advancing age.[16,17] A gradual increase in patients with respect to age was also observed in this study.

The most common age group presenting with AUB in this study was 41-50 years. Similar observations were also made by Doraiswami *et al*[16] and Jairajpuri *et al*.[18] An increased number of cases in this age group could be due to the fact that as menopause approaches, decreased number of ovarian follicles and their increased resistance to gonadotrophic stimulation, results in low level of oestrogen which cannot keep the normal endometrium growing.[19]

Histopathological examination of the endometrial biopsies and curettings revealed various patterns ranging from physiological to pathological lesions of the endometrium. In this study, proliferative and secretory endometriums were the two most common histopathological patterns which were seen in all the three age groups. Similar observation was made in a study by Abdullah *et al*.[20] Together, both these patterns were seen in 165 (40.94%) cases. Data from similar studies vary from 28.36% to 53.91%.[12,16,18,20-22]

Disordered proliferative pattern lies at one end of the spectrum of proliferative lesions of the endometrium that includes carcinoma at the other end with intervening stages of hyperplasias.[16] In this study, 54 (13.4%) cases were diagnosed while in the literature, its incidence varies from 5.7% to 20.54%.[16,18,20] Similar to other studies,[16,20] it was more common in the 41-50 age group.

Endometrial hyperplasia is a precursor of endometrial cancer. It is more commonly seen during the perimenopausal period.[23] The classification used by the World Health Organization (WHO) designates four different types of hyperplasia. Hyperplasia is classified as simple or complex based on the absence or presence of architectural abnormalities such as glandular complexity and crowding. They are further designated as atypical if they demonstrate nuclear atypia.[24,25]

In this study, hyperplasia was seen in 44 (10.92%) cases. Similar observations (9.1% and 10%) were made Abdullah *et al*,[20] Gredmark *et al*.[26] However, its incidence was lower (5.79%) in a study by Jairajpuri *et al*[18] and higher in studies by Baral *et al* (18.3%)[24] and Muzaffar *et al* (24.7%).[17] Similar to the data in other studies,[20,24] the incidence of hyperplasia peaked in the perimenopausal age group.

The present study shows the detection of endometrial cancer increases with age (Table-2). In this study, endometrial carcinoma was seen in 10 (2.48%) cases which was similar to that reported by Sarwar *et al* (2%).[27] Lower incidences of 0.4%[28] and 0.47%[18] have also been reported in the literature. Likewise, higher incidences of 3.33% and 4.4% have been reported by Mencalgia[29] and Doraiswami *et al*[16] respectively. As reported in the literature,[5,16,20,25] endometrial carcinoma was also commonly seen in the post menopausal age group in our study.

Effects of exogenous hormones (pill endometrium) were seen in 25 (6.2%) cases of AUB. In other studies its incidence was lower and varied from 1.7%- 4.81%.[17,18,24,25] As in other studies,[17,18,24,25] pill endometrium was commonly seen in our study in the reproductive and perimenopausal age groups.

Atrophic endometrium comprised of 19 (4.71%) cases of AUB and was most common in the postmenopausal women. In other studies,[12,16,18,20,22] its incidence varies from 1.1%-7%. The exact cause of bleeding in atrophic endometrium is not known. It is thought to be due to anatomic vascular variations or local abnormal defective local haemostatic mechanisms.[16]

Weakly proliferative endometrium was seen in 39 (9.68%) cases and was common in the reproductive and perimenopausal age groups. It represents an intermediate point between profound atrophy of total oestrogen deprivation and the normal proliferative phase response to cyclic oestrogen production.[30]

Chronic endometritis was diagnosed in 13 (3.23%) cases.

Higher incidence varying from 5.8 to 24% have been reported in the literature.[12,18,20,27] It is often as a result of intra-uterine contraceptive devices (IUCD), pregnancy and incomplete abortions.[18]

The other causes of AUB include 5 (1.24%) cases each of deficient luteal phase and endometrial polyp. Endometrial specimens were inadequate for evaluation in 24 (5.96%) cases. Those endometrial specimens labelled unsatisfactory for reporting showed scant amount of fragmented glands and stromal tissue and large areas of haemorrhage. Limited literature is available on the criteria for adequate and inadequate endometrial specimen.[18]

The endometrial biopsies and curettings on histopathology revealed various patterns ranging from normal endometrium to malignancy. Majority of the patients with AUB presented with normal cyclic endometrium, followed by disordered proliferative endometrium and hyperplasia. The incidence of endometrial hyperplasia and endometrial carcinoma were more common in the perimenopausal and postmenopausal women. Hence, histopathological evaluation of the endometrium is specially recommended in women of these age groups presenting with AUB, to rule out possibility of preneoplastic condition or malignancy.

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