Asian Pac. J. Health Sci., 2018; 5(3):31-36 e-ISSN: 2349-0659, p-ISSN: 2350-0964

Document heading doi: 10.21276/apjhs.2018.5.3.5 Original Article

Histopathological patterns in endometrial biopsy associated with abnormal uterine bleeding

Ashumi Gupta[1*], Karsing Paitiri[1], Anshu Gupta[2], Renu Gupta[3], Pratima Khare[4]

[1]Assistant Professor, Department of Pathology, Dr Baba Saheb Ambedkar Medical College and Hospital, Rohini, Delhi, India

[2]Associate Professor, Department of Pathology, Dr Baba Saheb Ambedkar Medical College and Hospital Rohini, Delhi, India

[3]Specialist,Department of Pathology, Dr Baba Saheb Ambedkar Medical College and Hospital Rohini, Delhi, India

[4]Specialist and Head, Department of Pathology, Dr Baba Saheb Ambedkar Medical College and Hospital,Rohini, Delhi, India

Received: 15-06-2018 / Revised: 02-07-2018 / Accepted: 22-07-2018

ABSTRACT

Abnormal uterine bleeding is one of the most common gyenocological problems that affects women worldwide. We studied patterns of endometrial biopsy pathology in abnormal uterine bleeding in a tertiary care hospital in a metropolitan city. Retrospective study of 518 cases of endometrial samples were studied in patients presenting with abnormal uterine bleeding. Clinical data and endometrial biopsy findings were recorded. The age of the patients varied, ranging from 18 years to 70 years. Maximum number of patients presented in the age group 40-49 years (49.2%), followed by 30-39 years (34.9%). The patients presented most commonly as menorrhagia (48.6%). Cyclical pattern was the most common finding on endometrial biopsy including secretory (33.4%) followed by proliferative pattern (31.3%), gestational causes (9.8%), endometrial hyperplasia (7.1%) chronic endometritis (4.0%), endometrial polyp (3.0%), irregular endometrium (4.2%), malignancy (1.7%) and atrophic endometrium (0.6%). Endometrial hyperplasias and malignancy were more frequently seen in patients presenting ≥40 yrs of age. Pregnancy associated causes of abnormal bleeding were more common in patients of reproductive age group i.e. <40yrs. Endometrial biopsy is the usual investigation performed in abnormal uterine bleeding and it can help to determine the etiology and decide the management in these cases. Patients in reproductive age group may have an underlying pregnancy associated cause of abnormal bleeding. Endometrial hyperplasia and malignancy must be excluded in patients presenting at or above 40 yrs of age.

Keywords: Endometrial biopsy, abnormal uterine bleeding, endometrial hyperplasia.

Introduction

Abnormal uterine bleeding is one of the commonest gynecolocogical problems. Menstrual disorders affect a significant proportion of women. [1,2]

**Correspondence*

Dr.Ashumi Gupta

Assistant Professor, Department of Pathology, Dr Baba Saheb Ambedkar Medical College and Hospital, Rohini, Delhi, India.

E Mail: ashumi.gupta@gmail.com

It can be due to disorders related to reproductive tract including structural causes and ovulatory dysfunction, systemic causes such as endocrinological disturbances, coagulopathy or iatrogenic causes. [3]

Etiology varies in patients depending to some extent on the age group affected i.e. reproductive, perimenopausal or post menopausal age group.

Endometrial biopsy is usually done to investigate the cause of abnormal uterine bleeding [4] and gives a lot of useful information that helps in deciding management of patients.

Materials and methods

This retrospective study was conducted in Baba Saheb Ambedkar Medical College and Hospital, a tertiary care teaching hospital in Delhi, over a period of 2 years 4 months from January 2014 to April 2016. A total of 518 cases of endometrial samples were studied, including endometrial biopsies, endometrial curettage and dilatation curettage, performed in patients presenting with abnormal uterine bleeding. Clinical details of patients were recorded from laboratory requisition slips including age and pattern of menstrual abnormality. Endometrial biopsies were reviewed, histopathological findings were recorded. Patients with leiomyoma, isolated cervical or vaginal pathology and hemostatic disorders were excluded from the study. Inadequate samples were excluded from the study. For statistical analysis, the patients were grouped according to age and comparative analysis was done.

Biopsies were received in 10% formalin and processed as routine histopathological specimens. Multiple sections were taken (4-6µm) from formalin fixed paraffin embedded tissue blocks, stained with haematoxylin and eosin (H&E), and subsequently microscopically examined by pathologist. Statistical analysis was performed using chi square test.

Results

A total of 518 cases presenting with abnormal uterine bleeding were included in the study. The age of the patients varied, ranging from 18 years to 70 years. Maximum number of patients presented in the age group 40-49 years (49.2%), followed by 30-39 years (34.9%). The patients presented [Table 1] most commonly as menorrhagia (48.6%), followed by metrorrhagia (29.7%), polymenorrrhagia (7.5%) and post menopausal bleeding (5.8%).

Endometrial biopsy [Table 2] revealed normal cyclical pattern of endometrium in 65.6% of cases including secretory endometrium (33.4%), proliferative endometrium (31.3%) and shed endometrium (1.0%). Pregnancy related abnormal bleeding accounted for 51 (9.8%) of cases. Endometrial hyperplasia [Fig 1,2] constituted 37 cases (7.1%) including simple hyperplasia (28 cases, 5.4%), atypical simple hyperplasia (6 cases, 1.2%) and complex atypical hyperplasia (3 cases, 0.6%). Chronic endometritis [Fig 3] was seen in 21 cases (4.0%), and endometrial polyp (16 cases, 3.0%). Irregular endometrium was seen in 22 (4.2%) cases. Atrophic endometrium was seen in 0.6% cases.

Malignancy was discovered as the cause of abnormal bleeding in 9 cases (1.7%) including adenocarcinoma [Fig 4] in 5 cases (1.0%), squamous cell carcinoma (3 cases, 0.6%), and poorly differentiated carcinoma in 1 case (0.2%). Exogenous hormone effect was noted in 19 cases (3.7%). Adenomyomatous polyp was seen in 3 cases (0.6%). 1 cases showed granulomatous endometritis (0.2%).

In patients below 40 yrs of age [Table 3],complications of pregnancy including abortions, retained products and molar pregnancy etc constituted nearly one fourth of cases (23.6%). Pregnancy associated causes of abnormal bleeding were significantly more common in patients of reproductive age group i.e. <40yrs, as compared to older patients (p value<0.05). Endometrial hyperplasias were found to be significantly more frequent in patients presenting ≥40 yrs of age as compared to patients presenting before 40 yrs of age (p value<0.05). Malignancy were seen more frequently in patients ≥40yrs age as compared to younger patients, though the difference was not statistically significant.

Table 1: Clinical presentation in patients of abnormal uterine bleeding

Presentation	N	%
Menorrhagia	252	48.6%
Metrorrhagia	154	29.7%
Polymenorrhagia	39	7.5%
Menometrorrhagia	25	4.8%
Continuous bleeding	9	1.7%
Polymenorrhoea	7	1.4%
Oligomenorrhoea	2	0.4%
Post menopausal bleeding	30	5.8%
Total	518	100%

Table 2: Endometrial biopsy in abnormal uterine bleeding

Histological finding		**N**	**%**
Cyclical endometrium	Secretory pattern	173	33.4%
	Proliferative pattern	162	31.3%
	Shed endometrium	5	1.0%
Chronic endometritis	Chronic nonspecific	20	3.9%
	Granulomatous	1	0.2%
Polyp	Endometrial polyp	13	2.5%
	Adenomyomatous polyp	3	0.6%
Irregular endometrium		19	3.7%
Exogenous hormone		22	4.25%
Pregnancy related		51	9.84%
Endometrial hyperplasia		37	7.14%
Malignancy		9	1.74%
Cystic atrophic endo		3	0.58%
		518	100%

Table 3: Endometrial biopsy pattern distribution according to age

Histological finding	**<40**	**40-49**	**>=50**	**Total**
Cycling endometrium	123	188	29	340
Endometritis	11	9	1	21
Polyp	8	5	3	16
Irregular endometrium	7	14	1	22
Exogenous hormone effect	9	6	4	19
Pregnancy related	46	5	0	51
Endo hyperplasia	9	25	3	37
Malignancy	1	3	5	9
Atrophic endometrium			3	3
	214	255	49	518
	41.3%	49.2%	9.5%	100.0%

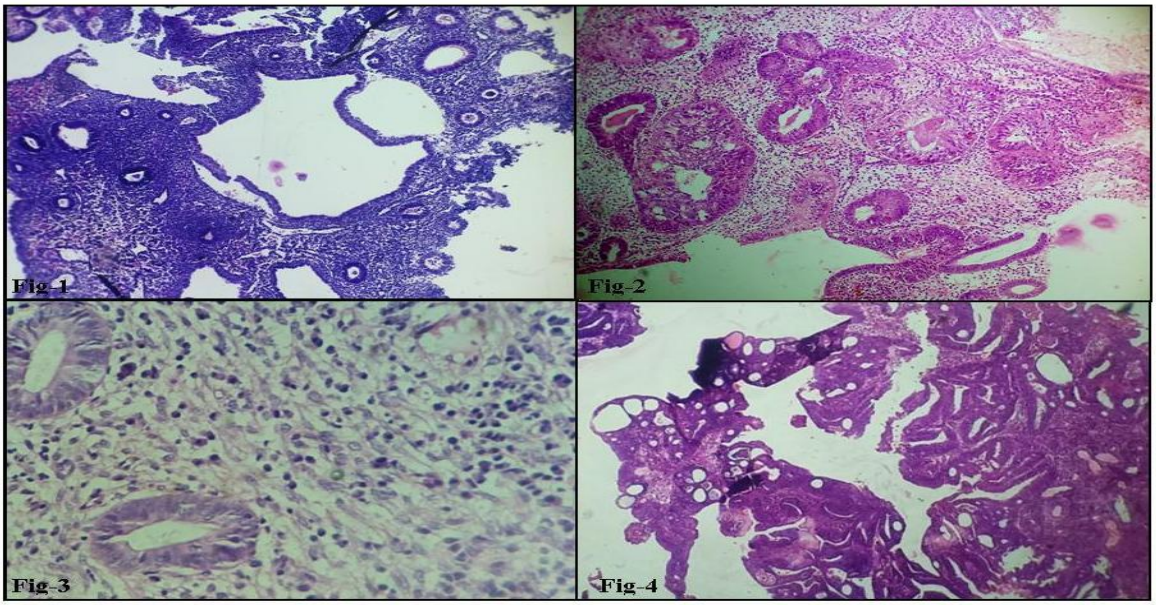

Fig 1:Simple hyperplasia without atypia (H&E stain x100)
Fig 2:Complex atypical hyperplasia (H&E stain x100)
Fig 3:Chronic endometritis (H&E stain x100), lymphocytes and plasma cells are seen in the endometrial stroma
Fig 4: Adenocarcinoma (H&E stain x100)

Discussion

Abnormal uterine bleeding is one of the most common problems encountered in gynaecological practice. It can present in various patterns including menorrhagia, polymenorrhoea, polymenorrhagia, metrorrhagia, menometrorrhagia and postmenopausal bleeding.
Different causes of abnormal bleeding occur in varying frequencies in different age groups. Recent PALM-COEIN classification approved by FIGO categorises the causes of abnormal uterine bleeding into structural and non structural namely – polyp, adenomyosis, leiomyoma, malignancy and hyperplasia; coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not yet classified. [3] Endometrial biopsy is frequently done in abnormal uterine bleeding, and it can give useful information regarding the cause of AUB. If the tissue obtained is scanty or devoid of stroma, it may be difficult to assess the biopsy. Artefactual appearances such as glandular crowding, telescoping may pose further problem in interpretation. [4]
Dysfunctional uterine bleeding (DUB) is the clinical term used when specific pathological, haematological and endocrine disorders have been excluded. In these cases, endogenous hormonal imbalance, including anovulatory cycles and luteal phase defect may lead to abnormal uterine bleeding. In cases of DUB, endometrial glands are usually non secretory type, with focal endometrial breakdown and features of chronic bleeding such as accumulation of foamy histiocytes, hemosiderin deposition and occasionally focal stromal fibrosis and hyalinisation. [4]
Menorrhagia is one of the common presentations of AUB. [6] In our study, patterns of abnormal bleeding included menorrhagia (48.6%), followed by metrorrhagia (29.7%), polymenorrrhagia (7.5%) and postmenopausal bleeding (5.8%). The age of the patients varied, ranging from 18 years to 70 years. Most frequent age group of presentation was 40-49 years (49.2%), followed by 30-39 years (34.9%), 50-59 years (8.1%) and 20-29 years (6.2%). Few cases presented at >60yrs age and in adolescent age group. We reported maximum number of patients with AUB in the 5^{th} decade followed by 4^{th} decade which is similar to other studies. [6,7] AUB presents with greater frequency in perimenopausal age group, [6,7] wherein menstrual cycles become anovulatory as the number of ovarian follicles diminish [4,7] and reduced progesterone levels lead to dysfunctional uterine bleeding in these cases. The endometrium usually shows proliferative pattern. DUB related to anovulatory cycles may also occur in perimenarchal adolescents, or in reproductive age group due to

polycystic ovarian disease or due to exogenous estrogen intake. [4]Estrogen related anovulatory bleeding can be either due to atresia of anovulatory follicles leading to estrogen withdrawal or because of overgrowth of endometrium in the face of persistent anovulatory follicles leading to breakthrough bleeding and irregular endometrial breakdown. Abnormal secretory pattern may be seen in progesterone related bleeding including luteal phase defect and irregular shedding. [5] Luteal phase defect may occur due to insufficient progesterone production or premature regression of corpus luteum following ovulation. [5] Histologically, the endometrium may appear to lag behind the actual date, or there may be a disparity between gland and stromal phase. [4] Some cases may show secretory pattern accompanied by stromal breakdown. Uncommonly, abnormal bleeding may occur due to irregular shedding wherein the endometrium shows mixed secretory and proliferative phase pattern or irregular secretory pattern with stromal breakdown. [5]

Most frequent biopsy finding in AUB is endometrium in normal cyclic phase i.e. secretory phase, proliferative phase and shedding endometrium. [6-9] In our study, secretory pattern (33.1%) was most common followed by proliferative endometrium (27.2%). Other studies have reported upto 30% endometrial biopsies with secretory pattern [10] and 26.2% with proliferative pattern [9] in AUB, which is comparable to our findings.

Pregnancy related complications are an important cause of uterine bleeding in the reproductive age group. [6,7] In patients below 40 yrs of age, complications of pregnancy including abortions, molar pregnancy etc constituted nearly one fourth of cases (23.6%). Looking at subgroup of patients below 30 years of age, pregnancy related complications emerged as the largest cause of abnormal bleeding (42.4%). In reproductive age group, abnormal uterine bleeding should prompt the clinician to exclude gestational causes before considering other etiology.

Endometrial hyperplasia was diagnosed in 37 cases (7.1%), which is similar to observations made by other authors. [11] Hyperplasia has been reported in endometrial biopsies with varied frequency in AUB, ranging from 5% to 18.3% [6-9]. Endometrial hyperplasia has been classified by the WHO previously on the basis of architectural complexity and cytological atypia – namely simple and complex hyperplasia with or without atypia respectively. [13] The new WHO classification recognizes hyperplasia into two categories namely endometrial hyperplasia without atypia and atypical endometrial hyperplasia/endometrioid intraepithelial neoplasia. [14] We recorded majority of endometrial hyperplasia cases without cytological atypia (75.67%) and 9 cases (24.32%) with atypia including simple atypical hyperplasia in 6 cases (16.21%) and complex atypical hyperplasia in 3 cases (8.10%). Endometrial hyperplasia was observed with greater frequency in patients >40 yrs of age (28/308 - 9.1%) as compared to patients <40yrs of age (9/215 – 4.18%). Maximum number of cases of endometrial hyerplasia occurred in patients 41-50yrs age (25/37, 67.56%), similar to other studies [7]. It is important to diagnose endometrial hyperplasia on biopsy as some of them may progress to carcinoma. Atypical endometrial hyperplasia has a higher risk of progression to endometrial carcinoma as compared to benign endometrial hyperplasia without atypia. [12] Endometrial biopsy revealed malignancy in 9 (1.7%) of cases, of which adenocarcinoma [Fig.3] was diagnosed in 5 cases (1%), squamous cell carcinoma in 3 cases (0.6%) and 1 cases revealed poorly differentiated carcinoma (0.2%). Other authors have reported a higher frequency of malignancy in AUB. [7-11] At times, it may be difficult to differentiate between low grade adenocarcinoma and atypical hyperplasia. Definite stromal invasion, may not always be seen on endometrial biopsies. However, presence of confluent glandular pattern without intervening stroma, infiltrating glands with surrounding desmoplastic stroma or extensive papillary pattern may indicate an underlying malignant pathology. [4,12]

Chronic endometritis was seen in 21 cases, 4.0% of cases. Granulomatous inflammation was seen in 1 case (0.2%). These findings are comparable with other studies. [7] Chronic endometritis shows the presence of plasma cells, usually surrounding the superficial endometrial glands. [4] Neutrophilic infiltrate is seen normally in menstrual endometrium. However, in presence of mononuclear inflammatory cells including plasma cells and lymphocytes it may indicate endometritis. Acute endometritis may be seen in absence of plasma cells such as in abnormal bleeding related to complications of pregnancy. [5] Endometrial polyps are a common cause of AUB and can be divided into hyperplastic, atrophic and functional patterns, and adenomyomatous polyp.[4] In this study, endometrial polyps were seen in 16 (3.05%) of cases including 3 cases(0.6%) with adenomyomatous polyp. Endometrial polyps have been associated with AUB with frequency ranging from 1.7% to as high as 33%. [6-11] Histopathological changes indicative of exogenous hormone effect were seen in 19 cases (3.6%). In another study, a lower incidence of pill endometrium was reported. [6], while some studies have reported a

higher incidence [8,15] Endometrial biopsies in patients receiving exogenous progesterone agents and combination preparations can show varied morphological patterns ranging from decidualisation, to secretory pattern or atrophic pattern. Sequential regimens may show weakly developed proliferative changes or secretory phase depending upon the timing of the biopsy. [5] Progestational agents when given in cases of hyperplasia may cause alteration in pretreatment morphology and the interpretation may be difficult. [5]Irregular endometrium was seen in 22 cases (4.2%), which is similar to other studies.[9] Atrophic endometrium was seen in 3 cases (0.57%). This incidence is lower than other studies.[6,8,9]

Conclusion

Abnormal menstrual bleeding can be due to a variety of endometrial causes. In reproductive age group, gestational causes are prominent. Majority of cases show cyclic endometrium. However, hyperplasia and malignancy are an important cause in perimenopausal and postmenopausal age groups and endometrial biopsy can provide crucial information for diagnosis and management of patients.

References

1. Bang RA, Bang AT, Baitule M, Choudhary Y, Sarmukadan S and Tale O: High prevalence of gynaecological diseases in rural Indian women. Lancet 1989; 1:85-87.
2. Latha, K, Kanani, SJ, Maitra, N. Prevalence of Clinically Detectable Gynaecological Morbidity in India: Results of Four Community Based Studies. The Journal of Family Welfare. Dec 1997; 43(4): 8-16.
3. Munro MG, Critchley HO, Broder MS, Fraser IS. FIGO working group on menstrual disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. Int J Gynecol Obstet. 2011;113(1):3-13.
4. McCluggage, W. Glenn: Benign Diseases of the Endometrium. In: Kurman, Robert J, Hedrick Ellenson, Lora Ronnet, Brigitte M, editors, Blaustein's Pathology of the Female Genital Tract. 6th ed. New York: Springer;2011. p. 305-358.
5. Mazur Michael T (et al.). Dysfunctional uterine bleeding. In Mazur Michael, Kurman Robert J**.** Diagnosis of endometrial biopsies and curretings. A practical approach. 2nd ed. New York: Springer; 2005. p. 100-120
6. Jairajpuri ZS, Rana S and Jetley S. Atypical uterine bleeding-Histopathological audit of endometrium. A study of 638 cases. Al Ameen J Med Sc i 2013;6(1) :21-28.
7. Doraiswami S, Johnson T, Rao S, Rajkumar A, Vijayaraghavan J, Panicker VK. Study of Endometrial Pathology in Abnormal Uterine Bleeding. J Obstet Gynecol India. 2011;61(4):426-30.
8. Vaidya S, Lakhey M, Vaidya S, Sharma PK, Hirachand S, Lama S, KC S. Histopathological pattern of abnormal uterine bleeding in endometrial biopsies. Nepal Med Coll J. 2013;15(1):74-7.
9. Bhatta S, Sinha AK. Histopathological study of endometrium in abnormal uterine bleeding. Journal of Pathology of Nepal 2012;.2:297 -300.
10. Mirza T, Akram S, Mirza et al. Histopathological pattern of abnormal uterine bleeding in endometrial biopsies. J Basic Applid sci 2012; 114-1
11. Pessoa JN, Freitas AC, Guimaraes RA, Lima J, Dos Reis HL, Filho AC. Endometrial Assessment: When is it Necessary. J Clin Med Res. 2014;6(1):21-5
12. Wilson PC, Buza N, Hui P. Progression of endometrial hyperplasia: a revisit under the 2014 WHO classifications. Int J Clin Exp Pathol 2016;9(2):1617-25.
13. Tavassoli FA, Devilee P. (Eds.): World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs. IARC Press: Lyon; 200
14. Zaino R, Carinelli S G, Ellenson L H. Tumours of the uterine Corpus: epithelial Tumours and Precursors. In: Kurman RJ, Herrington CS et al. WHO Classification of Tumours of female Reproductive organs. IARC Press: Lyon; 2014. p. 125–126
15. Sajitha K, Shetty PK, Shetty KJ, Prasad KHL, Permi HS, Hegde P. Study of histopathological patterns of endometrium in abnormal uterine bleeding. CHRISMED J Health Res 2014;1(2):76-81.

Conflict of Interest: None
Source of Support: Nil