Endometrial Evaluation in Abnormal Uterine Bleeding in a Tertiary Care Hospital – A 5 Year Retrospective Study

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ABSTRACT

BACKGROUND

Abnormal uterine bleeding (AUB) is one of the commonest presenting symptoms in gynaecological outpatient department (OPD). This term is used to describe irregular bleeding with no specific cause. Histopathological evaluation of endometrium plays a significant role in the diagnosis and its management. We wanted to study the frequent patterns of endometrium and evaluate the causes of bleeding and its association with age.

METHODS

This is a retrospective study done in the Department of Pathology, Government Medical College, Shivamogga, Karnataka, India, for a period of 5 years, from September 2012 - September 2017. All the endometrial samples received from gynaecological OPD of patients clinically diagnosed as AUB were included in the study. Data of these patients were retrieved from hospital records and records from pathology department. Those patients with known causes of bleeding were excluded from the study. Samples obtained were routinely processed, stained with haematoxylin & eosin (H & E) and examined microscopically. The data collected were entered in Microsoft Excel and analysed using SPSS software. Results were expressed in terms of percentage and proportions.

RESULTS

A total of 967 patients was included in our study. The age group of these patients ranged from 21 to 80 years. Majority of the patients belonged to 41 - 50 years age group (49.1 %), followed by 31 - 40 years (33.1 %) and the least number of cases was seen in the age group of 71 - 80 years (0.5 %). The most common bleeding pattern in women presenting with AUB was menorrhagia (48.2 %) followed by metrorrhagia (22.4 %), polymenorrhoea (15.4 %), menometrorrhagia (9 %) and metropathia haemorrhagica (4.8 %). The most common histopathological finding was proliferative phase (54.3 %) followed by secretory phase (17.3 %). Endometrial malignancy was detected in (2.4 %).

CONCLUSIONS

Histopathological evaluation of endometrium in AUB is crucial thereby facilitates accurate diagnosis and management.

KEYWORDS

Endometrium, AUB, Histopathology

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BACKGROUND

Uterus is a hollow, pear shaped organ which is divided into cervix and corpus. Uterine cavity is triangular in shape and lined by endometrial mucosa surrounded by myometrium and serosa. Endometrial mucosa is made up of glands and stroma. It is divided into a deeply situated basal layer and superficial functional layer. The basal layer is responsible for regeneration of the endometrium following menstruation. The functional layer is subdivided into 2 strata: compactum and spongiosum. The stroma is composed of endometrial stromal cells and blood vessels.[1] A normal endometrial cycle is associated with changes in both endometrial glands and stroma that allow the pathologist to diagnose microscopically the phase of menstrual cycle.[2]

Endometrium is a dynamic tissue that undergoes physiologic and characteristic morphologic changes during the menstrual cycle as a result of the effect of sex steroid hormones. "Dating" the endometrium by its histologic appearance is frequently used clinically to assess hormonal status, document ovulation and determine causes of endometrial bleeding and infertility.[3]

In general, the changes are quite uniform throughout the endometrium. The basal layer of endometrium is not subject to the influence of progesterone. Similarly, the mucosa of lower uterine segment responds only sluggishly to the hormonal stimulation.[1]

The endometrium is in a dynamic state of proliferation, differentiation and shedding, during active reproductive life. This cycle is exquisitely monitored by the pituitary and ovarian hormones. Abnormalities in this system lead to abnormal uterine bleeding.[3]

Abnormal uterine bleeding is one of the commonest presenting complaints affecting women of reproductive age in the gynaecological outpatient department. In today's era women experiencing AUB is relatively more, probably due to decreased parity / reduction of lactational amenorrhea.[4,5] AUB is defined as bleeding from uterine corpus that is abnormal in volume, regularity and timing and has been present for more than past six months[5]. There are both organic and functional causes of AUB. Functional causes of AUB constitute dysfunctional uterine bleeding (DUB) which is defined as pathological bleeding from uterus unexplained on the basis of inflammation, neoplasia or pregnancy within the uterus.[6]

In most instances, dysfunctional bleeding is due to the occurrence of an anovulatory cycle.

The most commonly employed endometrial sampling techniques are dilation and curettage and endometrial biopsy. Dilatation and curettage require anaesthesia and there is a small but definite risk of uterine perforation or secondary amenorrhoea. Endometrial biopsy in contrast is a relatively inexpensive office procedure with minimal complications. The endometrial sampling for abnormal bleeding should be undertaken during the bleeding episode. In general, progestational agents should not be administered before sampling, as these agents can mask important features necessary to identify abnormal endometrial proliferative states.

The importance of correlating the morphologic features of endometrial biopsy with the clinical findings cannot be overemphasized. The minimal clinical information required for interpretation in most cases, includes the patients' age, the date, characteristics of the last menstrual period, a statement about past or current administration of steroidal medication and an account of current chief complaint and physical findings.

Due to diversity of presentation of abnormal uterine bleeding, histopathological evaluation of endometrial biopsy plays a pivotal role in its diagnosis and management. This study was undertaken to determine the various histopathological patterns of endometrium in women of different age groups presenting with abnormal uterine bleeding.

METHODS

A retrospective study was done in the Department of Pathology, tertiary care teaching hospital over a period of 5 years from 2013 - 2017. All patients of reproductive age group who complained of abnormal uterine bleeding presented to gynaecologic outpatient department were taken up for the study. Complete history with regard to age, parity, fertility, socioeconomic status, amount and pattern of menstrual bleeding, last menstrual period, previous hormonal therapy and any other pelvic pathology were obtained. All the details were retrieved from hospital records and records in pathology department. Inclusion and exclusion criteria were as follows:

Inclusion Criteria

1. AUB of any type,
2. Patients belonging to reproductive age group (21 to 70 yrs.).

Exclusion Criteria

3. Pregnancy
4. Organic lesions of myometrium, cervix, vagina and adnexa.
5. Intra uterine foreign body (IUCD), coagulopathies / bleeding disorders, associated endocrine disorders.

The obstetricians performed general physical examination, pelvic and per speculum examination to rule out any palpable, organic, pelvic pathology. Routine investigations were done to rule out any causes of bleeding. These investigations included complete haemogram, coagulation profile, renal function test, liver function tests, random blood sugar, serum human chorionic gonadotropin (HCG) and ultrasonography. To rule out endocrine pathology, thyroid function test, follicle stimulating hormone (FSH), luteinizing hormone (LH) and prolactin levels were assessed. These patients underwent dilatation and curettage (D & C) / endometrial biopsy. The samples of endometrial tissue sent from outpatient department to histopathology lab

were labelled. The endometrial tissue was fixed in 10 % formalin for 12 - 24 hours and then entire tissue was subjected for routine tissue processing using paraffin embedding medium. Sections of thickness of 0.5 µm were taken from these paraffin blocks and stained with routine haematoxylin and eosin stain (H & E stain). These histopathological slides were retrieved from the department file and studied.

Statistical Analysis

Results obtained were tabulated and statistically analysed. The data were entered in Microsoft Excel and analysed using SPSS software. Results were expressed in terms of percentage and proportions.

RESULTS

A total of 967 samples of endometrium obtained from AUB patients were included in our study. The age group of these patients ranged from 21 - 80 years. Majority of the patients belonged to 41 - 50 years (49.1 %) followed by 31 - 40 years (33.1 %) and the least number of cases were seen in the age group of 71 - 80 years (0.5 %) (Table 1)

Age Group (Years)	Number of Cases	Percentage
21 - 30	101	10.40 %
31 - 40	320	33.10 %
41 - 50	475	49.10 %
51 - 60	39	4.00 %
61 - 70	26	2.70 %
71 - 80	6	0.50 %
Total	**967**	

Table 1. Age Distribution

Most common bleeding pattern in women presenting with abnormal uterine bleeding (AUB) was menorrhagia (48.2 %) followed by metrorrhagia (22.4 %), polymenorrhoea (15.4 %), menometrorrhagia (9 %) and metropathia haemorrhagica (4.8 %) (Table 2)

Bleeding Pattern	Number of Cases	Percentage
Menorrhagia	466	48.20 %
Metrorrhagia	217	22.4 %
Menometrorrhagia	87	9 %
Polymenorrhoea	151	15.6 %
Metropathia Haemorrhagica	46	4.8 %
Total	**967**	

Table 2. Bleeding Pattern

In our study, the most common histopathological finding of endometrium was proliferative phase (54.3 %) followed by secretory phase (17.3 %). Endometrial malignancy was detected in (2.4 %) (Table 3)

Histopathology	Total Number of Cases	%
Proliferative phase	525	54.3 %
Secretory phase	167	17.3 %
Simple hyperplasia	105	10.9 %
Endometrial carcinoma	23	2.4 %
Endometrial polyp	45	4.6 %
Atrophic endometrium	22	3.8 %
Endometritis	12	1.2 %
Complex hyperplasia with atypia	14	1.5 %
Luteal phase defect	10	1.1 %
Disordered proliferative endometrium	12	1.2 %
Complex hyperplasia without atypia	22	3.8 %
Pill endometrium	10	1.1 %
Total	**967**	

Table 3. Histopathological Pattern of Endometrium

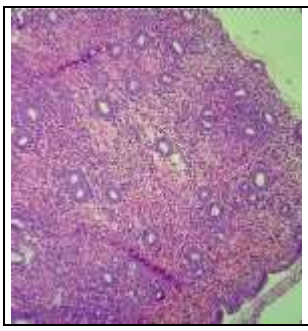

Figure 1. Proliferative Phase- Endometrium (H & E, 40x10)

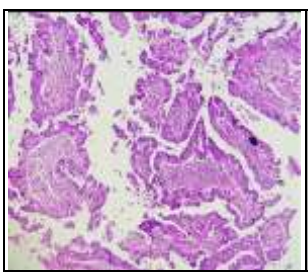

Figure 2. Endometrial Adenocarcinoma (H & E, 40x10)

DISCUSSION

Abnormal menstrual bleeding is the cause of worry, social embarrassment and disturbance of a healthy lifestyle, affecting millions of women globally. It is one of the most common and challenging problems faced by the gynaecologists. 9 - 14 % of the women between menarche and menopause present with abnormal uterine bleeding.[7]

The causes of AUB can be categorised in to two broad groups:

1. Organic causes-genital tract infections, tumours, adenomyosis, iatrogenic and systemic disorders – In about 25 % of the patients, well defined organic cause leads to abnormal uterine bleeding.
2. Functional causes also referred to as dysfunctional uterine bleeding (DUB) – It is the diagnosis of exclusion made when there is no recognisable medical cause.

Causes of abnormal uterine bleeding have been categorised by the Federation of International Gynaecology and Obstetrics (FIGO) in to new classification system (PALM-COEIN), which includes polyps, adenomyosis, leiomyoma, malignancy / hyperplasia, coagulopathy, ovulatory dysfunction, endometrial cause, iatrogenic cause, not yet classified.[5]

In our study, majority of AUB cases (49.1 %) were found in the age group of 41 - 50 years. This was similar to the study done by Singh A et al.[8], Nayak et al.[9], and Saraswathi D et al.[10]

The most common type of menstrual bleeding in the present study was menorrhagia (48.2 %). Similar results were validated by Singh A et al. (42 %) and Loganathan et al.[11] (35.5 %).

In the present study, most common histopathological pattern of endometrium was proliferative phase (54.3 %) followed by secretory phase (17.3 %) which is consistent with the study done by Mehta K et al.[12] (52 % and 18 %) and Khan S[13] (46.4 % and 38.4 %).

On microscopy, endometrial glands in early proliferative phase show round and short tubular glands lined by cuboidal

to columnar epithelium surrounded by a compact stroma. Mid proliferative phase showed curved, long glands. Late proliferative phase showed tortuous glands with pseudo stratification. Stroma showed mitotic activity and compact cellularity. (Fig 1).[10,11]

Early secretory endometrium showed subnuclear vacuolation of the glandular epithelium. Stroma showed moderate oedema. Mid secretory endometrium is characterised by coiled secretory glands lined by round, vesicular nucleus. Many glands show luminal secretions. Stroma showed marked oedema. Late secretory endometrial glands show irregular, serrated glands. These glands are closely packed with minimal stromal oedema. Stroma showed marked predecidual change and marked spiral arterioles.

The term endometrial hyperplasia denotes a proliferative endometrium featuring glandular architectural abnormalities that result in glandular crowding and takes the form of either cystic dilatation of glands (simple hyperplasia) or glandular budding (complex hyperplasia).

In our study, simple hyperplasia constituted 10.9 % which was in accordance with the study done by Bhoomika et al.[2] (12 %) and Mehta K et al.[12] (9 %). As stated by Nayak et al.[9] range of simple hyperplasia varies from 7 - 34.6 %. The reason for this variation is attributed to socio economic status, obesity, diabetes, sedentary lifestyle and early diagnosis.

In simple hyperplasia, gland to stromal ratio is increased. Glands are of various sizes and lined by columnar epithelium with variable degree of stratification and nuclear atypia. Many glands show cystic dilatation filled with secretions. Stroma is cellular and compact.

In the current study, complex hyperplasia without atypia comprised of 3.8 % and complex hyperplasia with atypia was 1.5 %. This was similar to the study done by Nayak et al.[6] which showed 3.1 % and 1.9 % respectively.

Complex hyperplasia shows hyperplastic glands with increased gland to stromal ratio. Glands are crowded and are arranged back to back with very little intervening stroma. These glands show highly complex architecture with budding and intra luminal papillary folding and are lined by columnar cells showing stratification and increased mitotic activity with or without atypia.[12]

The criteria for atypical hyperplasia include nuclear enlargement and very often nuclear rounding, some degree of pleomorphism, loss of nuclear polarity and a shift in the nuclear cytoplasmic ratio. Other features present include prominent nucleoli, nuclear irregularity, clumped chromatin and atypical mitotic figures.

Benign endometrial polyp was found in 4.6 % of all the cases. This is in correlation with the study done by Khan R et al.[14]

Endometrial polyp is a grossly pedunculated lesion whose stalk is composed of collagenous fibrous stroma populated by cystically dilated and occasionally crowded glands lined by inactive, atrophic to weakly proliferative endometrium. The central portion of a polyp contains large, thick walled coiled blood vessels.

On histopathology, polyp is composed of a polypoidal structure lined by tall columnar epithelium overlying tubular and cystically dilated glands surrounded by a fibrotic stroma with thick walled congested blood vessels.[15]

Endometrial adenocarcinoma constituted 2.4 % which was comparable with the study done by Singh A et al.[8] (1 %) and Nayak et al.[9] (1.25 %).

Grossly, endometrial carcinoma shows large, polypoidal / papillary / irregular friable grey white growth extending into the adjoining structures variably. Endometrial adenocarcinomas are divided into endometrioid (usual type) and special variant types.

On microscopy, the endometrioid type of tumour is composed of large, architecturally complex macro glands or closely approximated back to back arranged micro glands or exophytic, thin stalked, branching papillary pattern (villoglandular pattern) with scant intervening stroma. Tumour also shows variable degrees of haemorrhage, necrosis, lymphoplasmacytic infiltrate and lymphovascular emboli. Based on differentiation, tumour can be graded as Grade I (well differentiated) to Grade III (poorly differentiated).

Tumour cells show high nuclear-cytoplasmic (N / C) ratio, hyperchromatic nuclei, high mitotic figures, and moderate to abundant eosinophilic to vacuolated cytoplasm. Cells are seen infiltrating into the surrounding stroma and myometrium (Fig 2). Various types of metaplasia are a common finding.[14]

Special variants of endometrial adenocarcinoma include serous carcinoma, clear cell carcinoma, mucinous carcinoma, pure squamous cell carcinoma, mixed carcinoma and undifferentiated carcinoma.

Atrophic endometrium accounted for 3.8 % in our study. Atrophic endometrium refers to appearance of the epithelium lining the endometrial glands. The epithelium tends to be mitotically inactive and bland cytologically. Microscopy shows thinned out endometrium with few tiny glands lined by inactive, cuboidal epithelium and few cystically dilated glands surrounded by a stroma containing small spindle cells which exhibits varying degree of collagenisation and no mitotic activity.[16]

In our study, endometritis comprised of 1.2 %. It is classified as acute endometritis, non-specific chronic endometritis and granulomatous endometritis. Acute endometritis shows diffuse infiltration of glands and stroma by neutrophils and presence of micro abscesses as well as infiltration and destruction of glandular epithelium. In non-specific chronic endometritis, glands are infiltrated by large number of lymphocytes, plasma cells and lymphoid follicles with germinal centres. The characteristic finding is presence of plasma cells. Xanthomatous endometritis is a form of chronic endometritis characterised by sheets of xanthoma cells. Granulomatous endometritis can be focal or diffuse. When it is focal it indicates local pathology, while diffuse lesions imply systemic disease. In India, most common cause is tuberculosis. The other causes of granulomatous endometritis are idiopathic, sarcoidosis, etc. It shows epithelioid granulomas with or without caseation comprising of aggregates of epithelioid cells, Langhan's type of giant cells surrounded by lymphocytes and fibroblasts.[15]

Disordered proliferative endometrium accounted for 1.2 % in this study. Disordered proliferative endometrium show

dyssynchronous development of glands within easily discernible stroma. This is common in anovulatory cycles particularly in perimenopausal years. Biopsy shows widely spaced, variable shaped glands, few showing cystic dilatation and shallow budding surrounded by an easily discernible compact stroma.

Luteal phase defect comprised of 1.1 % in our study. This is a condition arising from inadequate corpus luteum resulting in low progesterone output. Progesterone deficiency may be absolute or relative. Absolute deficiency may have various causes like primary ovarian defect, central defect with insufficient FSH or LH stimulation. Relative progesterone deficiency is caused due to delayed ovulation or repeated anovulatory cycles. Microscopy showed secretory endometrium lagging the characteristics expected at that date. On histopathology, endometrium shows widely spaced poorly convoluted glands, a variation in the development of glands and stroma from region to region (discordant glands and stroma).[17] Pill endometrium accounted 1.1 % in the present study. Histopathology shows endometrial glands which are strikingly small and atrophic glands in a decidualised stroma.[17] Endometrial biopsy is an innocuous, efficient diagnostic tool in the evaluation of abnormal uterine bleeding. Histopathological examination of endometrium helps to exclude the local causes and establishes the diagnosis of DUB and thereby facilitating the mode of management.

CONCLUSIONS

Abnormal uterine bleeding is a common crippling condition in women of reproductive age group. Endometrial evaluation is crucial especially in perimenopausal and postmenopausal women to rule out local causes, premalignant conditions and malignancy. Histopathological evaluation of endometrium remains the gold standard for managing patients with abnormal uterine bleeding, as it reveals a broad spectrum of changes from normal proliferative / secretory endometrium to endometrial malignancy.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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REFERENCES

[1] Gilks B. Uterus: Corpus. Rosai and Ackerman's Surgical Pathology. 11th edn. Elsevier Publication 2018: p. 1302-1316.
[2] Norris HJ, Hertig AT, Abell MR. The Uterus. Baltimore: Williams and Wilkins 1973.
[3] Ellenson HL, Pirog CE. Female genital tract: functional endometrial disorders. Robbins and Cotran pathologic basis of disease. 8th edn. Elsevier Publication 2010: p. 1026-1034.
[4] Dadhania B, Dhruva G, Agravat A, et al. Histopathological study of endometrium in dysfunctional uterine bleeding. Int J Res Med 2013;2(1):22-24.
[5] Munro MG, Critchley HOD, Broder MS, et al. FIGO classification system for causes of abnormal uterine bleeding in non-gravid women of reproductive age. Int J Gnecol Obstet 2011;113(1):3-13.
[6] Khan PK. Dysfunctional uterine bleeding. J Obstet Gynecol India 1964;14:348-354.
[7] Mary GS, Tarin AS, Patrice MW. Evaluation and management of abnormal uterine bleeding in premenopausal women. Am Fam Physician 2012;85(1):35-43.
[8] Singh A, Bai RPV. Study of histopathological pattern in endometrium in abnormal uterine bleeding and its management. Int J Reprod Contracept Obstet Gynecol 2016;5(2):432-436.
[9] Nayak AK, Hazra K, Jain MK. Clinico-pathological evaluation of dysfunctional uterine bleeding. International Journal of Contemporary Medical Research 2017;4(4):920-924.
[10] Saraswathi D, Thanka J, Shalinee R, et al. Study of endometrial pathology in abnormal uterine bleeding. J Obstet and Gynecol India 2011;61(4):426-430.
[11] Loganathan M, Krishnakumar M. Histopathological study of endometrium in dysfunctional uterine bleeding. Int J Reprod Contracept Obstet Gynecol 2018;7(9):3497-3501.
[12] Mehta K, Jalandhara J, Kumavat A. Histopathological study of endometrium in dysfunctional uterine bleeding. Int J Medical and Health Research 2018;4(12):76-78.
[13] Khan S, Hameed S, Umber A. Histopathological pattern of endometrium on diagnostic D&C in patients with Abnormal uterine bleeding. Annals of King Edward Medical University 2011;17(2):166-170.
[14] Khan R, Sherwani RK, Rana S, et al. Clinico-pathological patterns in women with dysfunctional uterine bleeding. Iran J Pathol 2016;11(1):20-26.
[15] Longacre AT. The uterine corpus. Sternberg's Diagnostic surgical pathology. 5th edn. Lippincott Williams and Wilkins 2010: p. 2184-2212.
[16] Berek JS. Berek's and Novak's Gynaecology. Dysfunctional uterine bleeding in different age groups. 14th edn. Lippincott Williams and Wilkins 2007.
[17] Hellweg GD. Histopathology of the endometrium. 4th edn. Springer Verlag 1987.