Histopathological Evaluation of Endometrium in Cases of Abnormal Uterine Bleeding- An Institutional Experience in a Tertiary Care Center

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ABSTRACT

BACKGROUND
Abnormal Uterine Bleeding (AUB) is defined as any bleeding that does not correspond with the frequency, duration or amount of blood flow of a normal menstrual cycle. It is the commonest presenting symptom and major gynaecological problem responsible for as many as one-third of all outpatient gynaecologic visit**.** Aim of the present study was to find out the histopathological pattern of endometrium in Abnormal Uterine Bleeding (AUB).

METHODS
Specimens received as endometrial curettage, and hysterectomy specimens were studied followed by correlation of histopathology with age, parity and clinical presentation.

RESULTS
The patients were mainly from the age group of 41 - 50 years (43.25%). Most of the patients were multiparous (81.2%). The most common menstrual disorder was menorrhagia (57.12%). In abnormal uterine bleeding the most common histological pattern of endometrium was proliferative endometrium (38.7%) followed by secretory phase (22.1%) and disordered proliferative endometrium (13.3%). Endometrial carcinoma cases were 0.5% and there was one case (0.2%) of carcinosarcoma.

CONCLUSIONS
Histological study of endometrium, along with a thorough clinical history and detailed physical examination, should be promptly done for every case of abnormal uterine bleeding, especially in peri- and post-menopausal women.

KEYWORDS
Abnormal Uterine Bleeding, Menorrhagia, Endometrial Hyperplasia, Carcinosarcoma

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BACKGROUND

The endometrium which lines the uterine cavity is one of the most dynamic tissues in the human body; an interesting tissue for histopathological study. It is characterized by cyclic processes of cell proliferation, differentiation and death in response to sex steroids elaborated in the ovary.[1] Abnormal uterine bleeding is the commonest presenting symptom and major gynaecological problem responsible for as many as one-third of all outpatient gynaecologic visit.[2] Menorrhagia affects 10-30% of menstruating women at any one time, and may occur at some time during the perimenopause in up to 50% of women.[3] Abnormal Uterine Bleeding (AUB) is defined as any bleeding that does not correspond with the frequency, duration or amount of blood flow of a normal menstrual cycle.[4] It is a common problem and could be a sign of simple hormonal imbalance or a serious underlying condition necessitating aggressive treatment including a major surgical procedure.[5]

The endometrial sampling is chosen to evaluate abnormal uterine bleeding because it has several advantages over other diagnostic methods. The hormonal assay is very expensive and laboratories with hormonal assay are not available in rural areas. Ultrasonography clearly depicts the uterine contour and the status of the ovary, but fails to provide adequate information regarding the endometrium, except in atrophy and hyperplasia.[6] Very few lesions escape detection by D&C, especially as hysteroscopy has almost replaced blind curettage so that the uterine cavity can be observed and the area in question can be curetted.[7] The only disadvantage of endometrial biopsy is that, it is an invasive procedure. The underlying abnormality can be detected by histological variations of endometrium taking into account the age of the woman, the phase of her menstrual cycle, and use of any exogenous hormones. An understanding of the normal morphological appearance of the endometrium provides an essential background for the evaluation of endometrial pathology.[1]

The present study was a prospective study undertaken in the Department of Pathology, M.K.C.G. Medical College & Hospital to evaluate histopathology of endometrium for identifying the causes of abnormal uterine bleeding and to observe the incidence of various pathology in different age groups.

METHODS

The present study was a prospective study conducted in the Department of Pathology, MKCG Medical College, Berhampur, Odisha, from 2013 to 2015. A total of 548 endometrial samples received in the Pathology department of clinically diagnosed cases of AUB were histomorphologically studied. Detailed clinical history was collected from the patients along with all relevant investigations.

Inclusion Criteria

Reproductive women in all age groups attending the department of OB & G with abnormal uterine bleeding whose endometrial sample (both D&C and hysterectomy) were sent to the Department of Pathology.

Exclusion Criteria

Women with pregnancy complications, acute pelvic inflammatory disease, abnormal cervical pap smear, previous abnormal endometrial biopsy, leiomyoma, haemostatic disorders and women on hormonal treatment for abnormal uterine bleeding were excluded.

The material obtained was fixed in 10% formalin, followed by standard grossing techniques. The samples obtained by dilatation and curettage were all embedded and in hysterectomy specimens, the representative areas are taken and processed. Multiple bits were given wherever necessary.

Out of total 548 specimens, 221 were hysterectomy and 327 were D&C specimens which were processed in automated tissue processor and 3-5-micron thick sections were stained with Haematoxylin and Eosin (H & E). Microscopic examination and histopathological reporting was done by two histopathologists. Various endometrial patterns were classified as follows: Proliferative, Secretory, Atrophic, Unsatisfactory, Chronic Endometritis, Polyp, Submucosal Leiomyoma, Hyperplasia and Carcinoma. Endometrial Hyperplasia was classified according to World Health Organization (WHO), originally proposed by Kurman & Norris, into simple and complex on the basis of architecture and each was further subdivided into typical and atypical, based on cytology.[8] Data was collected and analysed.

RESULTS

The present study comprises of evaluation of histopathological findings of 548 clinically diagnosed cases of AUB which were received at the department of pathology, MKCG Medical College, Berhampur. The study was conducted over a period of 24 months.

The age of patients in the present study ranged from 17 to 77 years. The maximum number of cases was seen in the age group of 41-50 years (43.25%) and minimum number was seen in the age group of ≤20 years (1.6%). (Table 1) The parity ranged from 0 to 6 in the present study. The incidence of AUB was found to be highest in multiparous (52.9%) women followed by grand multiparous (28.3%) and least in nulliparous women (18.8%). (Table 2) Heavy menstrual bleeding was the most common symptom accounting for 57.12% of patients followed by postmenopausal bleeding accounting for 16.23% with the least being menometrorrhagia (2.74%). (Table 3)

Proliferative phase was the most common histological finding accounting for 38.7% followed by secretory phase accounting for 22.1 and disordered proliferative

endometrium 13.3% and the least commonly seen were complex hyperplasia with atypia 1.3%, complex hyperplasia without atypia 1.1%, endometrial adenocarcinoma 0.5% & carcinosarcoma 0.2%. We received 7 endometrial samples that could not be categorized due to inadequacy of material, but as per the published data of several authors,[7,9,10] we included those cases in our study. (Table 4)

Age Group (in Years)	No.	%
≤20	9	1.6
21-30	71	12.95
31-40	155	28.3
41-50	237	43.25
>50	76	13.9
Total	548	100

Table 1. Age Distribution Pattern

Parity	No.	%
Nulliparous	103	18.8
Multiparous (1-3)	290	52.9
Grand Multiparous (>3)	155	28.3
Total	548	100

Table 2. Relationship of AUB with Parity

Bleeding Patterns	No.	%
Heavy bleeding (Menorrhagia)	313	57.12
Intermenstrual Bleeding (Metrorrhagia)	67	12.23
Heavy & prolonged bleeding (Menometrorrhagia)	15	2.74
Frequent menstrual bleeding (Polymenorrhoea)	43	7.85
Oligomenorrhea	21	3.83
Post-menopausal bleeding	89	16.23
Total	548	100

Table 3. Distribution of Bleeding Patterns

Histological Findings	No.	%
Proliferative endometrium	212	38.7
Secretory endometrium	121	22.1
Chronic endometritis	18	3.3
Simple hyperplasia without atypia	23	4.2
Complex hyperplasia without atypia	6	1.1
Complex hyperplasia with atypia	7	1.3
Endometrial polyp	29	5.3
Disordered proliferative endometrium	73	13.3
Atrophic endometrium	48	8.7
Endometrial adenocarcinoma	3	0.5
Carcinosarcoma	1	0.2
Inadequate	7	1.3
Total	548	100

Table 4. Analysis of Histopathological Findings

All the cases were categorized into reproductive (15-40 years), perimenopausal (41-50 years) and postmenopausal (>50 years) groups; done in accordance to studies by several authors.[3,10,11] There were 226 patients belonging to the reproductive age group (21-40 years). Proliferative endometrium was the dominant histological finding in this age group accounting for 51.8% followed by 32.3% of secretory endometrium; there were no cases of malignancy in this group. There were 246 patients belonging to the perimenopausal (41-50 years) age group. Proliferative endometrium was the dominant histological finding in this age group accounting for 33.8% followed by 21.1% of disordered proliferative endometrium. There were 5 cases (2.1%) of complex hyperplasia with atypia and 1 case (0.4%) of endometrial adenocarcinoma in this age group. There were 76 patients belonging to the postmenopausal age group (>50 years). All the histological patterns were seen in this group although atrophic endometrium was the dominant histopathological finding accounting for 38.2% followed by 23.7% of disordered proliferative endometrium and 11.9% of proliferative endometrium. 2 cases (2.6%) of endometrial adenocarcinoma & 1 case (1.3%) of carcinosarcoma (malignant mixed mullerian tumour) were seen.

DISCUSSION

Abnormal uterine bleeding continues to be one of the most common and perplexing problems in Gynaecological practice. Histopathological diagnosis of endometrial samples is paramount in identifying the various conditions causing AUB, since it could be a sign of a serious underlying condition necessitating aggressive treatment including a major surgical procedure.[5] The highest incidence of AUB was noted in the 41-50 years age group in the present study which is in concordance with the results of the studies by Anusuya Dass[12] and Doraiswami Saraswathi,[13] whereas Bhattacharji[14] reported maximum incidence in 31-40 years age group and Srestha S[10] reported maximum incidence in 21-30 years age group. Considering these discrepant observations, one may conclude that, any age after menarche is not exempt from AUB.

Histological Findings	Khan S[15]		Bhatta S[9]		Shilpa[16]		Sharma J[11]		Present Study	
	No.	%	No.	%	No.	%	No.	%	No.	%
Proliferative Endometrium	233	46.6	32	26.23	70	35.0	86	44.1	212	38.7
Secretory Endometrium	192	38.4	20	16.39	53	26.5	17	8.7	121	22.1
SH without atypia	32	6.4	22	18.03	48	24.0	38	19.47	23	4.2
SH with atypia	12	2.4	-	-	-	-	-	-	-	-
CH without atypia	14	2.8	-	-	-	-			6	1.1
CH with atypia	-	-	-	-	3	1.5	10	5.1	7	1.3
Disordered proliferative endometrium	-	-	8	6.56	6	3	13	6.66	73	13.3
Endometrial polyp	3	0.6	3	2.46	4	2	2	1.02	29	5.3
Atrophic endometrium	5	1.0	9	7.38	7	3.5	12	6.15	48	8.7
Endometritis	2	0.4	8	6.56	-	-	2	1.02	18	3.3
Hormone effect	-	-	-	-	-	-	14	7.27	-	-
Endometrial adenocarcinoma	2	0.4	7	5.74	2	1	1	0.51	3	0.5
Endometrial stroma sarcoma	-	-	-	-	1	0.5	-	-	-	-
Carcinosarcoma	-	-	-	-	-	-	-	-	1	0.2
Inadequate	-	-	8	6.56	-	-	-	-	7	1.3
Total	500	100	122	100	200	100	195	100	548	100

Table 5. Comparative Analysis of Histopathological Findings

The present study significantly revealed that the occurrence of menstrual disorders increases with advancing age. The high incidence in the 41-50 years age group (43.25%) could be due to the fact that as menopause approaches, decreased number of ovarian follicles & increased resistance to gonadotrophic stimulation results in a low level of oestrogen which cannot keep the normal endometrium growing.[8] The incidence of AUB in above 50 years group was lower as compared to those between 41 and 50 years. The reason for this finding may be due to the fact that the patients were evaluated much earlier and treated appropriately thereby decreasing the incidence in later age group.

In the present study, the highest incidence of AUB was seen in multiparous women (52.9%), which is in concordance with the results of the studies by Bhattacharji[14] (46%), Sadia K[15] (54%) and Shilpa[16] (58%). The lowest incidence was seen in nulliparous women in the present study (18.8%) which is in concordance with the results of the studies by Anusuya Dass[12] (18%), Bhattacharjee[14] (18.8%), Sadia K[15] (5.4%) and Shilpa[16] (12.5%). By these observations, it may be implied that the incidence of AUB is highest in parous women in general (81.2% in our study) and multipara in particular (52.9% in our study).

In the present study, heavy menstrual bleeding was the commonest type of bleeding at presentation (57.12%), similar to findings in the studies by Shilpa[16] (60.5%) and Sharma J[11] (57.44%). A comparative analysis of histopathological findings is presented in Table 5. Predominant number of cases in this study showed normal physiologic phases such as proliferative, secretory and atrophic endometrial patterns; this is similar to findings by most other authors. The bleeding in the proliferative phase may be due to anovulatory cycles and bleeding in the secretory phase is due to ovulatory dysfunctional uterine bleeding.[13]

In the present study, proliferative endometrium was found to be the most common (38.7%) histological pattern followed by secretory endometrium (22.1%). Khan S[15] (PE-233/46.6%, SE-192/38.4%) and Shilpa[16] (PE-70/35%, SE-53/26.5%) had similar findings. Chronic endometritis accounted for 3.3% of cases in the present study; Baral R[17] had similar finding (2.71%) in his study. The incidence of chronic endometritis is highly variable in different studies, from 0.64% (Sajitha K[7]) to 11.76% (Khare A[2]).

In the present study, incidence of atrophic endometrium was noted in 8.7% cases, which was similar to the finding by Bhatta S[9] (7.38%). The slightly high number of atrophic endometrium in our study can be explained by the high number of peri and post-menopausal women in our study, in comparison to other studies. Postmenopausal bleeding is frequently associated with an atrophic endometrium. Atrophy of endometrium occurs as a consequence of the prolonged absence of any endogenous or exogenous estrogenic stimulation. The thin atrophic endometrium is susceptible to minor injury and may be responsible for postmenopausal bleeding even in the absence of an identifiable lesion. Superficial large, dilated venules are situated under a thin endometrium which may rupture to cause excessive uterine bleeding.[18]

In the present study, a significant number of cases (13.3%) showed disordered proliferative endometrium in this study, which was close to the findings observed by Sajitha K[7] (12.2%). 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.[13] An earlier stage of presentation due to increased health awareness could explain the high incidence in our study, and this will be of definitive help to the practicing gynaecologists to prevent the disease progression.[13]

The incidence of endometrial hyperplasia in our study was 6.57% (Table 6), which was similar to the finding of Doraiswami S[13] (6.1%) and Srestha S[10] (5.8%); whereas the studies by Shah R[8] (42.9%) and Sajitha K[7] (25.0%) had a very high percentage of cases of endometrial hyperplasia. The relatively low incidence of endometrial hyperplasia in our study can possibly be explained by the fact that most of our patients belong to lower socioeconomic status and the occurrence of risk factors like obesity, diabetes, increased intake of animal fat and sedentary life style is low. Another reason could be that most of these patients are being identified at a much earlier stage, that is, in the disordered proliferative phase. Identification of endometrial hyperplasia is important because they are thought to be precursors of endometrial carcinoma.[13]

Authors	Year	No.	%
Doraiswami S[13]	2011	25/409	6.1
Sharma J[11]	2013	10/195	5.1
Srestha S[10]	2013	24/413	5.8
Shah R[8]	2014	163/380	42.9
Sajitha K[7]	2014	39/156	25.0
Present Study	2015	36/548	6.57

Table 6. Comparative Study of Incidence of Endometrial Hyperplasia in AUB

Endometrial polyps constituted 5.3% of all cases in our study, similar to the finding of Sajitha K[7] (5.12%). The study by Doraiswami S[13] had the maximum of 11.25% cases of endometrial polyp, whereas Sharma J[11] and Srestha S[10] had the minimum cases (1.02% and 1.45%, respectively).

In the present study, only 0.5% cases were of endometrial adenocarcinoma; (Table 7) Sharma J[11] had similar findings (0.51%). The incidence of endometrial adenocarcinoma varied from minimum 0.3% (Shah R[8]) up to 5.74% (Bhatta S[9]). Of the 3 cases of endometrial carcinoma in the present study, one case was in perimenopausal age group and two were in postmenopausal women. We also found one case of malignant mixed mullerian tumor and that was diagnosed in a 57 year woman with postmenopausal bleeding. The relatively low overall incidence of malignancy corresponds to the low incidence of endometrial hyperplasia in our study; and this could possibly be due to the same factors, as well as the practice of early childbearing and multiparity, as documented in a study by Dangal et al.[19]

Author	Year	No.	%
Doraiswami S[13]	2011	18/409	4.4
Khare A[2]	2012	3/187	1.6
Bhatta S[9]	2012	7/122	5.74
Sharma J[11]	2013	1/195	0.51
Srestha S[10]	2013	12/413	2.91
Shah R[8]	2014	1/380	0.3
Present Study	2014	3/548	0.5

Table 7. Comparative Study of Incidence of Endometrial Adenocarcinoma in AUB

CONCLUSIONS

Abnormal uterine bleeding is the most common presenting complaint in women regardless of age. AUB needs thorough

and prompt evaluation as it could be the only clinical manifestation of a serious underlying condition like endometrial cancer. Endometrial sampling is a simple, cost-effective and appropriate method that provides accurate diagnostic yield and could be effectively used as the first diagnostic step in abnormal uterine bleeding; although, at times its interpretation could be quite challenging to the practicing pathologist. Histopathological examination of endometrial biopsies in patients of abnormal uterine bleeding shows a wide spectrum of changes ranging from normal endometrium in various hormonal cycles to malignancy. Therefore histological study of endometrium, along with a thorough clinical history and detailed physical examination, needs to be promptly done for every case of abnormal uterine bleeding, especially in peri- and post-menopausal women.

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