

Histopathological correlation of endometrial samples in pre and postmenopausal women with abnormal uterine bleeding

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Abstract

Introduction: Abnormal Uterine Bleeding (AUB) is the most common clinical presentations in pre and postmenopausal women and is caused by various etiological factors ranging from inflammatory, benign to malignant lesions. The microscopical examination of the endometrium carries an important role in diagnosing various etiopathological factors in cases of AUB.

Objectives:

1. To know the spectrum of lesions of the endometrium with respect to age.
2. To determine histopathological correlation of endometrial samples in pre and postmenopausal women.

Materials and Methods: A cross sectional study was conducted from October 2009 to September 2011, involving 250 female patients, 40 years and above presenting with AUB. The patient's endometrial samples were collected by biopsy, D & C or hysterectomy.

Results: The maximum incidence of AUB in premenopausal women were seen in 40-42 years age group (38.42%), while in postmenopausal women, highest incidence of AUB cases were seen in the age group of 50-52(43.3%). years

In the present study there was a high association between histopathological spectrum of endometrial lesions and age. Proliferative pattern was the commonest endometrial profile in the age group of 50-54 years (30.31%), where as secretory pattern (30.29%) was common in the age group of 45-49 years, atrophic Endometrium (100%) is seen in the age group of 65-69 years, polyps (24.9%) in the age group of 60-64 years, endometritis (9.0%) in age group of 45-49 years, irregular shedding (21.6%) in the age group of 40-44 years, simple hyperplasia (19.6%) in the age group of 45-49 years, whereas endometrial adenocarcinoma was more frequent in the age group of 55-59 years (11.7%). In premenopausal women, the most common endometrial pattern was secretory (26.8%), while in postmenopausal women majority of the endometrial profiles were atrophic (41.7%).

Conclusion: This study showed that other than normal physiological changes in both pre and postmenopausal women, various benign and malignant conditions also occurred with increasing frequency. There was high association between the various bleeding presentations and spectrum of endometrium lesions found. Hence, the symptom "abnormal uterine bleeding", requires prompt attention with respect to the etiology whether physiological or pathological and cannot be ignored. Therefore, microscopic analysis of the endometrium must be considered in all elder women presenting with AUB.

Keywords: AUB, Endometrial histopathology, Pre and postmenopausal women.

Introduction

Abnormalities in menstruation are a common cause of general practice consultations in the primary or tertiary care centre¹. Endometrium is the mirror of hormonal status in a female.² Menstrual dysfunction continues to be a huge burden on the healthcare system with varying etiology and considerable social implications.

Abnormal uterine bleeding (AUB) has been defined as change in frequency of menses, duration of flow, or amount of blood loss. In adolescents, vaginal bleeding³ which occurs before menarche is abnormal, while in women of child bearing and premenopausal age, any change in menstrual period, frequency, duration or amount of flow, as well as bleeding between cycles, are considered as abnormal.

In post menopausal women, AUB is described as vaginal bleeding for 12 months or more, after the cessation of menses or unpredictable bleeding in those who have been receiving hormonal therapy for 12 months or more.⁴

Abnormal uterine bleeding can be a harbinger of sinister pelvic pathology or denote a relatively minor problem, therefore a thorough investigation into the problem is called for in every patient presenting with this complaint.⁵

The gold standard is hysteroscopy and endometrial biopsy, the latter which is usually the first step in the diagnosis of AUB, along with diagnostic endometrial curettage which is mandatory without delay in all cases of perimenopausal and postmenopausal bleeding to rule out malignancy. The microscopical examination of the endometrium plays an important role in diagnosing various etiopathological factors in cases of AUB.⁶

This study is therefore conducted to know the various endometrial lesions among pre and postmenopausal women with abnormal uterine bleeding in Navodaya Medical College Hospital and Research Centre, Raichur.

Aims and Objectives

1. To know the spectrum of lesions of the endometrium with respect to age.
2. To determine histopathological correlation of endometrial samples in pre and postmenopausal women.

Materials and Methods

Source of data:All female patients in the premenopausal group (45 + 5 years) and postmenopausal group (50 years and above) presenting with abnormal uterine bleeding, admitted in the inpatient ward of tertiary care hospital and from other peripheral referral centers, are the subjects of this study. A cross sectional study for a period of two years has been done.

Methods of collection of data:

Samples of the endometrial tissue were obtained by:

D and C

Endometrial Biopsy

Hysterectomy.

Detailed Requisition forms with clinical data of the study subjects were received along with samples of the endometrial tissue in 10% formalin bottles. The tissue samples were fixed in 10% formalin solution for 12 hours and prepared for microscopic examination by a series of Histopathology processes.

Inclusion criteria: All patients in the premenopausal group (45 + 5 years) and post menopausal group (50years and above) presenting with abnormal uterine bleeding.

Exclusion criteria:

1. Patients < 40 years of age.
2. Patients complaining of abnormal uterine bleeding due to non endometrial causes like lesions of the myometrium and adnexa.
3. Patients with uterine bleeding due to Intra –uterine Devices.
4. Patients presenting with abnormal uterine bleeding due to pregnancy and its related complications

Methods of Study

A prospective study of 250 AUB cases was conducted and the results were analyzed according to age and histopathological spectrum of endometrial lesions.

Descriptive statistics were applied according to variable (i.e), frequency and percentage were calculated for bleeding patterns and histopathological spectrum of endometrial lesions in 250 AUB cases. Maximum and minimum age of the study group was described and mean age was calculated. The data was expressed in proportion of Chi - square test(or Fisher's Exact test in case of a small sample) which was used to examine association between age, and histopathological spectrum of endometrial lesions. Avalue < 0.05 was considered as significant and 0.01 as highly significant.

Observations and Results

Age incidence of AUB cases in pre and menopausal women

A total number of 250 cases were enrolled in the study over a period of 2 years, out of which, 160 cases (64%) were premenopausal women and90 cases (36%) were postmenopausal women.

The Age incidence of the premenopausal women varied from 40 to 49 years with a mean(Standard deviation) age of 43.6 (+3) years. Highest number of patients wereseen between 40 to 42 years, whereas minimum were seen in 48 years and above age group and the same is shown below in the table.

Table 1: Age incidence of AUB cases in premenopausal women.

Age(in years)	Frequency(Cases)	Percentage (%)
40-42	73	38.42
43-45	61	32.10
46-48	30	15.78
>48	26	13.68
Total	190	100.0

Table 2: Age incidence of AUB cases in postmenopausal women

Age (in years)	Frequency(cases)	Percentage(%)
50-52	26	43.3
53-55	09	15.0
56-58	08	13.3
59-61	11	18.3
62-64	04	6.7
65-67	02	3.3
Total	60	100

Table 3: Age incidence of histopathological spectrum of endometrial lesions

Age in years	Proliferative	Secretory	Atrophic	Polyp endometritis	Endometritis	TB endometritis	Irregular shedding	Simple hyperplasia	Simple hyperplasia with cystic change	Complex hyperplasia	Adenocarcinoma	Stromal tumor	Total
40-44	36 (26.9)	35 (26.1)	3 (2.2)	6 (4.5)	7 (5.2)	1 (0.7)	29 (21.6)	11 (8.2)	5 (3.7)	1 (0.7)	0	0	134 (53.6)
45-49	11 (19.6)	17 (30.3)	2 (3.6)	4 (7.1)	5 (8.9)	1 (0.8)	5 (8.9)	7 (12.5)	4 (7.1)	0	0	0	56 (22.4)
50-54	10 (30.3)	3 (9.1)	7 (21.2)	1 (3.0)	0	1 (3.0)	6 (18.2)	0	2 (6.1)	1 (3.0)	1 (3.0)	1 (3.0)	33 (13.2)
55-59	1 (5.9)	0	10 (58.8)	2 (11.8)	0	0	1 (5.9)	1 (5.9)	0	0	2 (11.7)	0	17 (6.8)
60-64	0	0	6 (75.0)	2 (25.0)	0	0	0	0	0	0	0	0	8 (3.2)
65-69	0	0	2 (100)	0	0	0	0	0	0	0	0	0	2 (0.8)
Total	58 (23.2)	55 (22.0)	30 (12.0)	15 (6.0)	12 (4.8)	3 (1.2)	41 (16.4)	19 (7.6)	11 (4.4)	2 (0.8)	3 (1.2)	1 (0.4)	250 (100.0)

In the present study there was also a high association between histopathological spectrum of endometrial lesions and the age ($p < 0.0001$).

Proliferative pattern (30.29%) was the most common endometrial profile in the age group of 50-54 years, secretory pattern (30.3%) was common in the age group of 45-49 years, atrophic endometrium (100%) in the age group

of 65-69 years, polyps (25%) in the age group of 60-64 years, endometritis (8.9%) in age group of 45-49 years, irregular shedding (21.6%) in the age group of 40-44 years, simple hyperplasias (19.6%), in the age group of 45-49 years, whereas endometrial adenocarcinoma (11.7%) was more frequent in the age group of 55-59 years.

Table 4: Spectrum of endometrial lesions in pre and postmenopausal women.

S.no	Type of endometrium	Pre menopausal Women (n-190)	Percentage (%)	Post menopausal women (n-60)	Percentage (%)
1	Proliferative	47	24.7	11	18.3
2	Secretory	51	26.8	4	6.7
3	Atrophic	5	2.6	25	41.7
4	Polyps	10	5.3	5	8.3
5	Endometritis	12	6.3	0	0
6	TB Endometritis	2	1.1	1	1.7
7	Irregular shedding	33	17.4	8	13.3
8	Simple hyperplasia	18	9.5	1	1.7
9	Simple hyperplasia with cystic change	10	5.3	1	1.7
10	Complex hyperplasia	2	1.1	0	0
11	Adenocarcinoma	0	0	3	5
12	Stromal Tumor	0	0	1	1.7
	Total	190	100	60	100

Commonest endometrial pattern in premenopausal women, was secretory (26.8%), followed by proliferative (24.7%), irregular (17.4%), simple hyperplasia (14.8%) and endometritis (6.3%), whereas in postmenopausal women, majority of the endometrial profiles were atrophic (41.7%) followed by proliferative (18.3%), irregular shedding (13.3%), polyps (8.3%), secretory (6.7%) and adenocarcinoma of the endometrium (5%). The following table depicts endometrial profiles in pre and postmenopausal Women.

Discussion

Total number of 250 patients presented with abnormal uterine bleeding were included in the study.

Age incidence of AUB cases

The age incidence of the patients with abnormal uterine bleeding, varied from 40 to 67 years and maximum presentation was seen in the age group of 40 to 49 years (64%) in the present study, which correlated with studies conducted by Shekhar P⁷ and Tariq Sarfraz⁸

In this study, premenopausal women with AUB accounted to 64%, while postmenopausal women accounted to 36%, the findings of which varied with similar studies by Baral R⁹. who reported AUB in 46.6% of premenopausal and 4.6% postmenopausal women.

Incidence of various endometrial profiles in aub cases

In the present study, the incidence of various endometrial lesions in descending order of frequency were proliferative (23.2%), secretory (22%), irregular shedding (16.4%), atrophic (12%), simple hyperplasia (12%), polyps (6%), endometritis (4.8%), tuberculous endometritis (1.2%), endometrial adenocarcinoma (1.2%), complex hyperplasia (0.8%) and stromal tumour (0.4%).

Proliferative endometrial pattern (23.2%) which is the predominant endometrial profile in this study, correlated with the observations of Veena et al,⁶ in their similar study who also reported high incidence (30.8%), whereas the

incidence of the same in separate studies conducted by Muzaffar et al¹⁰ (25.8%) and Dungal G¹¹ (17.8%) were low, when compared to our study.

Irregular shedding in our study accounted to 16.4% of cases, where as the findings of Baral et al⁹ reported a high incidence (26.6%) in their study and lower incidences were documented by authors like Veena M et al⁶ (7.7%) and Muzaffar et al¹⁰ (0.8%). In the present study, the incidence of simple hyperplasia was 12% which was similar to the findings of Veena M et al⁶ (14.5%), Baral R et al⁹ (12.3%) and Dungal G¹¹ (10%), whereas the studies of Muzaffar et al¹⁰ (23.5%), showed comparatively higher incidence. Among the endometrial profiles in this study, endometritis (4.8%) was comparatively less common, the findings of which were consistent with that of Dungal G¹¹ in which they recorded 6%, but varied with the study conducted by Muzaffar et al¹⁰ which showed 13%.

Table 5: Comparison of spectrum of endometrial lesions in the present study with other studies

S.no	Type of endometrium	Veena M et al(1996) ⁶ (%)	Dungal G(2003) ¹¹ (%)	Muzaffar et al(2005) ¹⁰ (%)	Baral R et al(2001) ⁹ (%)	Present study(2011) (%)
1	Proliferative	30.8	17.8	25.8	16.0	23.2
2	Secretary	25.8	10.7	35.4	15.6	22.0
3	Atrophic	0.9	34.5	0.0	5.0	12.0
4	Polyps	2.9	0.0	1.2	1.3	6.0
5	Endometritis	0.9	6.0	13	2.6	4.8
6	TB Endometritis	3.8	0.0	0.0	0.0	1.2
7	Irregular shedding	7.7	0.0	0.8	26.6	16.4
8	Simple hyperplasia	14.5	6.0	8.5	12.3	7.6
9	Simple hyperplasia with cystic change	0.0	4.0	15	0.0	4.4
10	Complex hyperplasia	3.8	0.7	1.2	2.0	0.8
11	Adenocarcinoma	2.9	9.5	0.4	1.0	1.2
12	Stromal Tumor	0.9	0.0	0.0	0.0	0.4

The incidence of endometrial adenocarcinoma in the present study was very low(1.2%) and similar findings was noted in the studies conducted by Veena M et al⁶ (2.9%) and Baral R⁹ et al (1%). But, contradictory to our study Dungal G¹¹ reported a higher incidence (9.5%) of this lesion.

Age incidence of histopathological spectrum of endometrial lesions

There was high association between age and histopathological spectrum of endometrial lesions in our study subjects ($p < 0.0001$). Proliferative pattern was the most common endometrial profile occurring in the age group of 45-54 years (23.5%) in the present study, the findings of which were supportive in the study conducted by Archana Bhosle,¹² who reported 66.1% in the above mentioned age group, whereas Muzaffar et al¹⁰ in their study documented that, secretory profile (41.3%) was more common in the age group of 45-54 years.

In our study atrophic endometrium (41.7%) was seen commonly in the age group of 50 years and above, which was similarly observed by Ali Hassan et al¹³ (42%) and Narula¹⁴ (41.7%) in their studies, who reported a high incidence in the same age group.

Cases of irregular shedding of the endometrium (17.4%) in our study were seen occurring with increasing frequency in the age group of 40-49 years and was similar to the findings of Baral R et al⁹ (32%) in their study, who reported an increased incidence in the above age group.

In the present study, polyps (14.8%) were the next common among the endometrial lesions in the age group of 55 years and above, which corroborated with the study of Ali Hasan et al¹³ (17.9%), whereas, inflammatory conditions like endometritis (7.3%) was mostly seen in age group of 40-49 years, the supportive findings of which were seen in the studies conducted by Baral R⁹ (3%) and Muzaffar (11.1%) et al.¹⁰

Endometrial hyperplasia occurred more in the age group of 40-49 years (15.7%) in this study and this finding

corroborated with the study of Ali Hassan et al¹³ (31.25%), Baral R et al⁹ (29%), Danggal G¹¹ (23%) and (15.2%), but varied with the observations of Narula¹⁴ (15.2%), but varied with the observations of Narula¹⁴ (15.2%), Muzaffir et al¹⁰ (20%).

Table 6: Comparison of endometrial adenocarcinoma in the present study with various studies

Authors	Narula (1967) ¹⁴	Danggal G (2003) ¹¹	Muzaffir et al (2005) ¹⁰	Ali Hassan et al (2010) ¹³	Baral et al (2011) ⁹	Present study (2011)
Percentage %	31.25	23	20	15.2	29	15.7

The peak incidence of endometrial adenocarcinoma in the present study was seen in the age group of 55-59 years (11.7%) which almost correlated with the study conducted by Danggal G¹¹ (17.7%) and Ali Hassan¹³ (7.5%), whereas in

the study of Baral R et al⁹ there was a correlation with the age, but a higher incidence of this lesion was observed (21%).

Table 7: Comparison of endometrial adenocarcinoma in the present study with various studies.

Authors	Danggal G (2003) ¹¹	Ali Hassan et al (2010) ¹³	Baral et al (2011) ⁹	Present study (2011)
No of cases Percentage %	8(17.7)	7 (7.5)	3(21)	3(11.7)
Age group in years	>55	55-64	>55	55-59

Spectrum of endometrial lesions in pre and post menopausal women:

Premenopausal Women

In this study, in premenopausal women, the most common endometrial pattern was secretory (26.8%), followed by proliferative (24.7%), irregular shedding (17.4%), endometrial hyperplasia (15.9%), endometritis (6.3%) and polyps (5.3%). In premenopausal women, majority of the endometrial profiles were secretory (26.8%) and proliferative patterns (24.7%) which corroborated with the observations of Danggal G¹¹ (23% and 38.5%), but varied with the studies conducted by Muzaffir et al¹⁰ (18.5% and 14.1%) and Baral R et al⁹ (13% and 10%) who reported comparatively lower incidences.

The profile of irregular shedding in our study was 17.4%, which was higher than the findings of Baral R et al⁹ (6%) and Muzaffir et al¹⁰ (0.4%).

In the present study, cases of endometritis accounted to 6.3%, which was consistent with the studies of Muzaffir et al¹⁰ (6.8%), but a lower incidence was seen in the studies of Baral R⁹ (3%).

Polyps, in our study accounted to 5.3%, on the contrary to Muzaffir et al¹⁰ who reported a low incidence of 0.4%. In the present study, the incidence of endometrial hyperplasia was 15.9%, which was similar to the findings of Muzaffir et al¹⁰ (20%) and Danggal G¹¹ (23%) whereas, the studies of Baral R et al⁹ (29%), showed comparatively higher incidences.

Table 8: Incidence of Endometrial profiles in Premenopausal Women in present study and their Comparison with various studies.

Authors	Danggal G (2003) ¹¹	Muzaffir et al (2005) ¹⁰	Baral et al (2011) ⁹	Present study (2011)
Lesions	%	%	%	%
Proliferative	38.5	14.1	10.0	24.7
Secretory	23.0	18.5	13.0	26.8
Atrophic	0	0.0	3.0	2.6
Irregular shedding	0	0.4	6.0	17.4
Endometritis	0	6.8	3.0	6.3
Polyps	0	0.4	0.0	5.3
Endometrial hyperplasia	23.0	20.0	29.0	15.9

Postmenopausal Women

In postmenopausal women, majority of the endometrial profiles were atrophic (41.7%). This finding corroborated with the observations of Ali Hassan et al¹³, and Danggal G¹¹ the former who reported a high incidence of 42%, while the latter reported an incidence of 64.4%. The profile of irregular shedding in our study was 13.3%, which was similar to the findings of Baral R⁹ (14%). Polyps in our study accounted to 8.3% of cases, whereas a slightly higher

incidence (13.3%) was reported by Ali Hassan et al.¹³ Endometrial hyperplasia were less common (3.4%) in this study, the findings of which comparatively varied with the findings of Baral R et al⁹ and Ali Hassan et al¹³ who reported higher incidences of 21% and 13.2% respectively. A low incidence was seen in TB endometritis (1.7%) which corroborated with the observations of Nasira S et al¹⁵ (0.6%), while stromal sarcomas (1.7%) in the present study also occurred in low incidence, but varied with the study of Ashraf et al¹⁶ (16%) who reported a high incidence.

In the present study, all of the cases of endometrial adenocarcinoma (5%) presented in postmenopausal women, which was consistent with the studies of Ali Hassan et al¹³

(7.7%), but a higher incidence was seen in the studies of Baral R et al⁹ (21%) and Dangal G¹¹ (17.7%).

Table 9: Incidence of endometrial profiles in postmenopausal women in the present study and their comparison with various studies.

Authors	Dangal G (2003) ¹¹	Ashraf et al(2006) ¹⁶	Nasira et al(2010) ¹⁵	Ali hasan et al (2010) ¹³	Baral et al(2011) ⁹	Present study (2011)
Lesions	%	%	%	%	%	%
Proliferative	-	-	19.2	-	2	18.3
Secretory	-	-	4.5	-	1	6.7
Atrophic	64.4	-	21.2	42	5	41.7
Irregular shedding	-	-	1.9	-	14	13.3
Polyps	-	-	5.1	13.7	-	8.3
TB Endometritis	-	-	0.6	-	-	1.7
Endometrial hyperplasia	-	-	9.0	13.2	21	3.4
Endometrial Adenocarcinoma	17.7	-	8.3	7.7	21	5
Stromal tumor	-	16.0	-	-	-	1.7

Conclusion

The present study was undertaken firstly, to know the spectrum of lesions of the endometrium with respect to age and secondly, to determine various histological patterns of the endometrium in pre and postmenopausal women. This study showed that other than normal physiological changes in both pre and postmenopausal women, various benign and malignant conditions also occurred with increasing frequency. There was also high association between the various bleeding presentations and spectrum of endometrium lesions found. Hence, the symptom "abnormal uterine bleeding", requires prompt attention with respect to the etiology whether physiological or pathological and cannot be ignored. Therefore, microscopic analysis of the endometrium must be considered in all women over 40 years of age presenting with AUB. The categorization of the endometrial causes of AUB among pre and postmenopausal women has been hampered by applying inconsistent nomenclature, making it difficult to compare studies performed by different researchers, on homogenous populations of patients experiencing AUB.

Thus, for the development of a more extensive 'living' document that includes nomenclature of bleeding patterns, endometrial profiles and classifications of Abnormal Uterine Bleeding, these recommendations should be the starting point for further debate and research.

Conflict of Interest: None.

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