Histopathological evaluation of endometrium in pre and postmenopausal uterine bleeding.

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ABSTRACT
Introduction: Abnormal uterine bleeding is most common gynecological presentation in pre and postmenopausal women caused by benign and malignant lesions and infections. Histopathological examination is the gold standard in diagnosing exact cause of this bleeding.

Objectives: 1) To detect pattern of endometrium in women having abnormal uterine bleeding in pre and postmenopausal age group. 2) To detect incidence of carcinoma endometrium in this age group.

Methods: A retrospective study was conducted of 250 patients more than 40 years of age group presented with abnormal uterine bleeding from January 2011 to June 2014 attending R. D. Gardi medical college hospital Ujjain (M. P.). Histopathology reports of Endometrium were analysed and results were tabulated.

Results: Maximum incidence of AUB was found in the age group of 40-42 years premenopausal (38.42%) and 50-52 years in postmenopausal women (43.3%). Menorrhagia was most common bleeding pattern found in proliferative (28.5%) and secretory (28.5%) profile. Postmenopausal bleeding was common in atrophic endometrial profiles (41%) and malignant lesions (100%). Proliferative pattern was most common in age group of 50-54 years (30.3%), secretory in 45-49 years (30.3%), atrophic endometrium in age group 65-69 years (100%), polyp in 60-64years (25%), endometriosis (9.9%) in 45-49 years, irregular shedding (21.6%) in 40-44 age group, simple hyperplasia (19.6%) in 45-49 years, endometrial carcinoma (11.7%) in age group of 55-59 years.

Conclusion: Sampling of endometrium is a must in all women over the age of 40 years presenting with AUB for exact diagnosis of benign and malignant lesions

Key words: Abnormal uterine bleeding, Premenopausal and postmenopausal bleeding

INTRODUCTION
Abnormalities in menstruation are common complaints in gynecological patients. Endometrium is the mirror of hormonal status in a female. Menstrual dysfunction continues to be a huge burden on the healthcare system with varying etiology and considerable social implications. Menorrhagia in absence of local pathology is also common entity in gynecology. Every woman in her lifetime, experience, episodes of bleeding that will be perceived as abnormal. Abnormal uterine bleeding (AUB) has been defined as change in frequency of menses, duration of flow, or amount of blood loss. 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. Bleeding in postmenopausal woman is considered as abnormal and should be investigated right away. Abnormal uterine bleeding is classified into two broad categories. The first, due to organic causes like endometritis, myometritis, adenomyosis, leiomyomas, endometrial and cervical polyps, endometrial hyperplasia and malignant lesions of the endometrium and cervix, whereas the second category, is because of dysfunctional uterine bleeding, caused by anovulation. The term Dysfunctional Uterine Bleeding is defined as a state of abnormal uterine bleeding without any clinically detectable organic pathology and is a diagnosis by exclusion, which is made when there is no recognizable organic pathology. The spectrum of AUB comprises of menorrhagia, metrorrhagia, polymenorrhoea, polymenorrhagia, postmenopausal bleeding and postcoital bleeding. AUB can be caused by a wide variety of disorders, dysfunctional uterine bleeding is commonly responsible in premenopausal women, but in post menopausal women it is due to hormonal, bleeding diathesis, local pathology including infections, benign tumours and malignancy. In 3-10% of women of the reproductive age group with AUB, have infectious or reactive processes of the endometrium, like acute and chronic endometritis, while in 8-10% of premenopausal and postmenopausal women, endometrial polyps are a common cause of abnormal uterine bleeding. Premenopausal and postmenopausal women with endometrial hyperplasia who present with vaginal bleeding, accounts to approximately 5% of all cases of AUB and is due to endometrial hyperplasia, alterations in glandular architecture and changes in the gland – stroma ratio. In 90% of the patients with endometrial adenocarcinoma, abnormal uterine bleeding is commonly present and therefore, this
condition in a postmenopausal woman, warrants an initial evaluation of the patient for endometrial adenocarcinoma. 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 premenopausal and postmenopausal bleeding to rule out malignancy. The microscopical examination of the endometrium is the gold standard in diagnosing various etiological pathological factors in cases of AUB. This study is therefore conducted to know the spectrum of endometrial lesions among pre and postmenopausal women with abnormal uterine bleeding in R. D. Gardi medical college Ujjain.

AIMS AND OBJECTIVE
1) To find out pattern of endometrium in women having abnormal uterine bleeding in pre and postmenopausal age group.
2) To detect incidence of carcinoma endometrium in this age group.

MATERIAL AND METHODS
Retrospective study. Sample size was 250 women attending in patients of CRGH Hospital in R. D. Gardi medical college, Ujjain (M.P.) from January 2011 to June 2014 from Ujjain district.

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

Exclusion Criteria: 1. Patients less than 40 years of age. 2. Patients presenting with 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 related complications. Endometrium which was obtained from D&C and hysterectomy specimens, collected in formalin bulb sent for histopathological examination was studied. The results were tabulated according to age, bleeding pattern, and histopathological spectrum of endometrial lesions. Descriptive statistics applied according to variable. Data was expressed in proportion of Chi-square test (fisher’s exact test in small sample) which was used to examine association between age, bleeding pattern, and HP spectrum of endometrial lesion. A value <0.05 was considered as significant and 0.01 as highly significant.

RESULTS
A total number Of 250 cases were enrolled in the study over a period of 3 and ½ years, from January 2011 to June 2014, out of which, 160 cases (64%) were premenopausal and 90 cases (36%) were postmenopausal women.

| 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              | 100.0          |
Fig. 1: Incidence of Various Bleeding Patterns in Cases Presenting with AUB

![Pie chart showing incidence of various bleeding patterns.]

**INCIDENCE**
- MENORRHAGIA: 52 cases
- METRORRHAGIA: 24 cases
- POLYMENORRHAGIA: 4 cases
- POLYMENORRHOEA: 15 cases
- POST MENOPAUSAL BLEEDING: 5 cases

Fig. 2: Incidence of Various Endometrial Profiles in AUB Cases

**INCIDENCE OF VARIOUS ENDOMETRIAL PROFILES IN AUB CASES**
- PROLIFERATIVE: 23.2%
- SECRETORY: 16.4%
- ATROPHIC: 4.8%
- POLYPS: 4.4%
- ENDOMETRITIS: 2.0%
- TB ENDOMETRITIS: 1.2%
- IRREGULAR SHEDDING: 1.2%
- SIMPLE HYPERPLASIA: 6.0%
- SIMPLE HYPERPLASIA WITH CYSTIC CHANGE: 1.2%
- COMPLEX HYPERPLASIA: 12.0%
- ADENOCARCINOMA: 22.0%
- STROMAL TUMOUR: 0.4%
**DISCUSSION**

Age incidence of the patients with AUB varied from 40-67 years and maximum incidence was seen in the age group of 40-49 years (64%) in the present study which correlated with studies conducted by Shekhar P and Tarique Sarfaraz.

In this study, premenopausal women with AUB accounted to 64% while postmenopausal women to 36%, the finding of which varied with similar studies by Baral R, who reported AUB in 46.6% of premenopausal and 4.6% postmenopausal women. In the present study, incidence of various bleeding patterns according to decreasing order of frequency was menorrhagia in 52% cases, postmenopausal bleeding in 24% cases, metrorrhagia in 14.8% cases, polymenorrhoea in 5.2%, polymenorrhagia in 4% cases. Menorrhagia which was the predominant bleeding pattern in this study, was consistent with the findings of similar studies conducted by Muzzafir et al and Nayak et al, who reported incidence of 51.9% and 49.1% respectively. But the incidence of this bleeding pattern was slightly lower when compared to our study in studies conducted by Veena Maheshwari (41.3%) and Sagar S (40.9%). Post menopausal bleeding in our study was the second most common bleeding pattern (24%) and was slightly higher in incidence, when compared to other studies of Sagar S (10.1%).
Sulpurkar\textsuperscript{19} (8%), Veena et al\textsuperscript{19} (9.6%) and Nayak et al\textsuperscript{18} (12.9%).

Proliferative Endometrial pattern 23.2% which is a predominant lesion in our study correlated with observations of Veena et al\textsuperscript{19} (30.8%) whereas the incidence was low in studies of Muzaffir et al\textsuperscript{17} (25.8%) and Dangal G\textsuperscript{20} (17.8%). Irregular shedding (16.4%) whereas in Baral et al\textsuperscript{16} (26.6%) and lower incidences in Veena et al\textsuperscript{19} (7.7%) and Muzaffir et al\textsuperscript{17} (0.8%). The peak incidence of endometrial carcinoma was seen in the age group of 55-59 years (11.7%) which correlated with study of Dangal G\textsuperscript{20} (17.7%) and Ali Hassan\textsuperscript{21} (7.5%). In this study there is a high association between the various bleeding patterns and histopathological spectrum of endometrial lesions (p<0.0001). Menorrhagia was the most common pattern in this study, found in proliferative (28.5%) and secretory (28.5%), while the less common lesions were endometrial hyperplasias, irregular shedding, endometritis, polyps, and TB endometritis accounting for 15.2%, 13.8%, 5.4%, 4.6% 0.8% of cases respectively. These findings correlated with the study conducted by Veena et al\textsuperscript{19} in which menorrhagia as proliferative (34.9%), secretory (29.1%) and endometrial hyperplasias, irregular shedding, endometritis and polyps which accounted to 20.9%, 6.9%, 2.4%, 4.7% respectively.

The incidence of Tuberculous endometritis in relation to menorrhagia was low (0.8%), when compared to the study of Mridula Bose\textsuperscript{23} (19%). In the present study, postmenopausal bleeding was seen mostly in atrophied endometrium profiles (41.7%) while it was comparatively less in cases of malignant lesions (6.7%). These findings corroborated with the observations of Ali Hassan et al\textsuperscript{21} who reported high incidence of the above mentioned bleeding pattern in atrophic endometrium (42%) and low incidence in malignancies (7.8%). Contrary to these findings, Veena M et al\textsuperscript{19} reported a high incidence of malignant lesions (40%) and comparatively low incidence of atrophic (10%) profile in relation to postmenopausal bleeding. Baral R et al\textsuperscript{16} also stated in his study that, postmenopausal bleeding was more commonly associated with malignant lesions (21%). In this study metrorrhagia was seen most commonly in cases with irregular shedding (29.7%), while it was comparatively less in cases with endometritis (8.1%), polyps(5.4%), atrophic (2.7%) and TB endometritis (2.7%). These findings correlated with study of Muzaffir et al\textsuperscript{17} who reported a similar incidence of this bleeding pattern in polyps (2.9%) and endometritis (13.8%), whereas varied with irregular shedding (0.9%). The observations of Veena M et al\textsuperscript{19} (1.3%), correlated with our study with respect to atrophic pattern. Polymenorrhoea, in the present study was the dominant bleeding pattern in cases presenting with secretory (30.7%), irregular shedding (23.1%) and hyperplastic (23.1%) profiles and common in proliferative (15.4%) and endometritis (7.7%) which correlated with the observations of Muzaffir et al\textsuperscript{17} who documented similar incidence of secretory (41.6%) and endometritis (12.5%). On the contrary to Veena M et al\textsuperscript{19} in their study reported high incidence of proliferative (50%), followed by secretory (21%), hyperplasia (14.2%) and irregular shedding (7.1%). In this study in premenopausal women, the most common endometrial pattern was secretory (26.8%) and proliferative patterns (24.7%) which corroborated with the observations of Dangal G\textsuperscript{20} (23% and 38.5%) but varied with studies conducted by Muzaffir et al\textsuperscript{17} (18.5 and 14.1%). The profile of irregular shedding in our study was 17.4% which was higher than the findings of Baral R et al\textsuperscript{16} (6%) and Muzaffir et al\textsuperscript{17} (0.4%).

In post-menopausal women, majority of the endometrial profiles were atrophic(41.7%). This correlated with Ali Hassan et al\textsuperscript{21} (42%) and Dangal G\textsuperscript{20} (64.4%). The profile of irregular shedding (13.3%) was similar to Baral R\textsuperscript{16} (14%). Polyps (8.3%) and endometrial hyperplasia (3.4%) was higher in the study conducted by Ali Hassan et al\textsuperscript{21} (13.3% and 13.2% respectively). In the present study all cases of endometrial adenocarcinoma (5%) presented in post-menopausal women which was consistent with the studies of Ali Hassan et al\textsuperscript{21} (7.7%), but a higher incidence was seen in the studies of Baral R et al\textsuperscript{16} (21%) and Dangal G\textsuperscript{20} (17.7%). A case of tuberculous endometritis was seen in the patient of 54 years presenting with postmenopausal bleeding which is an uncommon presentation for this endometrial profile and the same was noted in the study conducted by Julio C et al\textsuperscript{24}. A rare case of malignant endometrial stromal tumour was included in the present study, seen in a 53 year old woman who presented with postmenopausal bleeding and a similar case presentation was noted by Cheung et al\textsuperscript{25}.

**CONCLUSION**

The present study was undertaken firstly to know the spectrum of lesions of the endometrium with respect to age and clinical features. Secondly to determine various histological patterns of endometrium in pre and postmenopausal women. Hence, the symptom “abnormal uterine bleeding” requires prompt attention with respect to 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.
REFERENCES