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Evaluation of Histopathological Spectrum of Post-Menopausal Bleeding among Women: A Cross Sectional Study

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ABSTRACT
Identification of postmenopausal bleeding in community settings provide an opportunity to detect these women at early stages of cancers. Histopathology is the gold standard tool used for the evaluation of the causes of post-menopausal bleed. The present study was carried out to determine the causes of postmenopausal bleeding and to differentiating various benign and malignant lesions based on histopathology findings. This cross sectional observational study was conducted in the department of pathology in a tertiary care center of India. A total of 200 cervical or endometrial biopsy samples were received in our histopathology section from post-menopausal bleeding women. Histopathological examination was done and findings are recorded in the form of benign and malignant lesions from all the samples. The majority of the patients (36%) were reported in the age group of 46 50 years with an average age of 53.6 years. Cervix was the most common site of biopsy (43%) followed by endometrial curettage (30%). Most of the cases were benign (53%) and 37.5% were malignant lesions on the basis of histopathological diagnosis. Atrophic endometrium (35%) followed by Proliferative endometrium (20%) were the common among benign lesion whereas., endometrial hyperplasia with atypia (12.5%) and endometrial carcinoma (5.5%) were common among malignant lesions in PMB cases. Postmenopausal bleeding etiology was predominantly benign in nature, atrophic endometrium., proliferative endometrium and endometrial hyperplasia were the most common histopathological findings of PMB cases.

INTRODUCTION

Menopause is taken from the Greek word "Meno" (month) and "pause" means stop. Menopause occurs physiologically in women who are about the age of fifty. Most women all over the world attain menopause at 45-55 yrs with the average age 51 yrs[1]. Postmenopausal bleeding (PMB) is defined as abnormal uterine bleeding occurring after 1 year of permanent cessation of menstruation resulting from loss of ovarian follicular activity[2]. Post-menopausal bleeding (PMB) is one of the most often referred conditions to gynecological services, owing to the possibility of an underlying endometrial cancer[3]. PMB has been de ned by WHO, as an episode of bleeding in 12 months or more after the last menses. In general population, the incidence of postmenopausal bleeding is approximately 10% immediately after menopause and 5% in all menopausal women[4]. Endometrial atrophy is the most prevalent endometrial abnormality in women experiencing post-menopausal bleeding, accounting for 60-80% of cases. Polyps that go unnoticed and untreated might cause recurring or continuous bleeding, resulting in a needless hysterectomy[5,6]. Various patterns of abnormal uterine bleeding were reported like, metrorrhagia, menorrhagia, dysfunctional uterine bleeding, menometrorrhagia and postmenopausal bleeding (PMB)[7]. Aetiology of the PMB includes benign and malignant causes, benign are cyclical endometrium and abnormal physiological changes of endometrium (disordered proliferative and atrophic endometrium) whereas among malignant lesions: endometrial hyperplasia, carcinomas, uterine polyp and pregnancy related complications were common[8]. Type I EC has an endometrioid histology and account for 70-80% of endometrial carcinomas. Type II EC has non endometrioid histology and arise in women who are less likely to have the clinical associations as seen in Type I cancers[9]. Although postmenopausal bleeding is often associated with benign pathology, the possibility of having an underline malignancy makes it a sinister complaint requiring thorough clinical work up. Evidence has shown that early detection of cervical and endometrial cancer improves the cure rate and reduces mortality[10]. Therefore, PMB requires complete assessment to ensure the absence of malignancy and to identify and treat high risk patients. Most studies on PMB are based on endometrial biopsies. The aim of the study was to evaluate the causes of postmenopausal bleeding based on Histopathological ending among post menopausal women attending our hospital.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Pathology in a tertiary care hospital, central India. All endometrial or cervical biopsy samples of post menopausal women received in our histopathology section during the study period were analysed.

Inclusion Criteria:

- Women ≥40 years of age.
- Post menopausal women complaint of bleeding attended our hospital.
- Women who gave written informed consent for the study.

Exclusion Criteria:

- Women aged <40 years.
- PMW with a vaginal bleeding arising from a cervical or vaginal or vulvar disease.
- Women with bleeding disorders, on anticoagulants on menopausal hormone therapy (MHT).
- Patients who not willing for the study.

All cases data were recovered from history, socio-demographic characteristics, clinical compliant and provisional diagnosis mentioned on patients requisition form. All relevant blood investigation and transvaginal sonography was done in all cases. Various biopsy samples like endometrial and cervical biopsy or hysterectomy specimens were received in our histopathology section. All biopsy samples were process for gross and histopathological examination as per the standard guidelines.

Biopsy tissue samples cut into very thin layers small pieces, called cut sections. Then, they stained with Hematoxylin and Eosin and examine under the microscope for histopathological evaluation of benign and malignant lesions. The histopathological findings were compiled, analysed and compared to other studies.

Statistical Analysis: Data were summarized using standard descriptive methods, frequency and percentages for categorical variables and mean and SD or median and range for continuous variables. Chi-square test and student's t test were performed for analysis of variance, $P<0.05$ were considered statistically significant

RESULTS AND DISCUSSIONS

A total 200 cases of postmenopausal bleeding women were enrolled and analysed in the present study. The majority of the cases (36%) were 46 50 year's age group with mean age being 53.6 years. Most of them (57%) residing in urban area, 53% were belong to middle socio-economic class and 56% had normal weight women. Duration of menopause was 1-5 year in most (52%) of the women. The PMB were maximum (55%) in multiparous patients (parity 1 3). Details shown in (Table 1).

Table 1: Basic Characteristics of Women with Postmenopausal Bleeding.

Basic Characteristics		Frequency (%)
Age Groups	41-45 years	10 (5%)
	46-50 years	72 (36%)
	51-55 years	54 (27%)
	56-60 years	44 (22%)
	>60 years	20 (10%)
Residing Area	Rural	86 (43%)
	Urban	114 (57%)
Socio-Economic Class	Lower	78 (39%)
	Middle	106 (53%)
	Upper	16 (8%)
Parity	Nullipara	8 (4%)
	Para 1-3	110 (55%)
	Para >3	82 (41%)
Duration of Menopause	<1 year	74 (37%)
	1-5 years	104 (52%)
	>5 years	22 (11%)
BMI	Normal	112 (56%)
	Overweight	67 (33.5%)
	Obese	21 (10.5%)

Cervix was the most common site of biopsy (43%) followed by endometrial curettage (30%), cervix and endometrium (10%) and hysterectomy with adenexa was in 7%. Details shown in (Fig. 2).

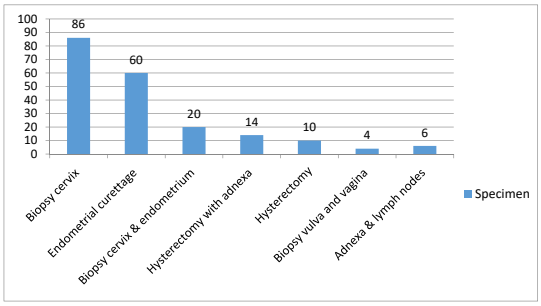


Fig. 1: Type of Specimens Collected from the Study Participants

Among histopathological diagnosis majority of the postmenopausal bleeding (53%) due to benign causes, 37.5% were malignant causes and rest 9.5% were premalignant (Fig. 2).

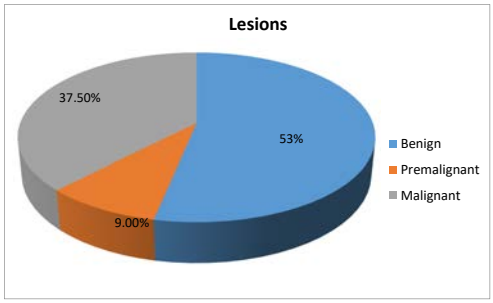


Fig. 2: Distribution of Lesions on the Basis of Histopathology among PMB Women

On the basis of histopathology findings endometrial lesions were categorized into Functional and Organic group. Atrophic endometrium (35%) followed by Proliferative endometrium (20%) were the common among functional lesion whereas., endometrial hyperplasia (12.5%) was common among organic lesions. Detail description was shown in (Table: 2).

Table 2: Distribution of Histopathological Finding in Post Menopausal Bleeding Women.

Histopathology Diagnosis	Frequency	Percentage
Atrophic Endometrium	70	35%
Proliferative Endometrium	40	20%
Secretory Endometrium	15	7.5%
Disordered Proliferative Endometrium	11	5.5%
Endometritis	8	4%
Endometrial Polyp	5	2.5%
Endometrial Hyperplasia	25	12.5%
Carcinoma in situ of cervix	6	3%
Endometrial Hyperplasia with Atypia	4	2%
Endometrial Carcinoma	11	5.5%
Unremarkable	5	2.5%

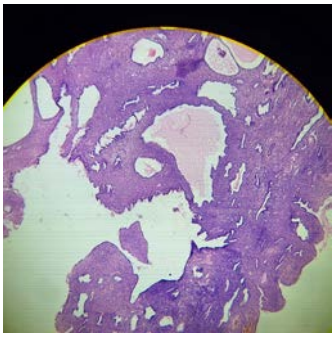


Image 1: Benign Endometrial Polyp

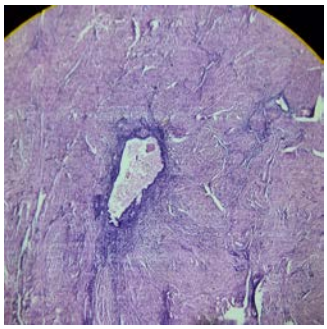


Image 2: Adenomyosis

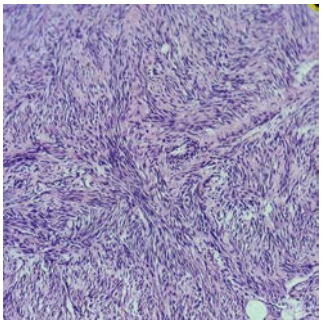


Image 3: Leiomyoma

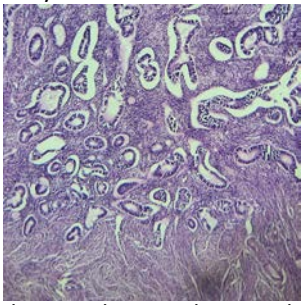


Image 4: Endometrial Hyperplasia Without Atypia

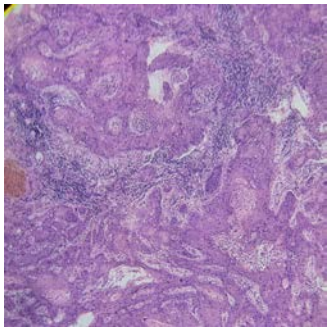
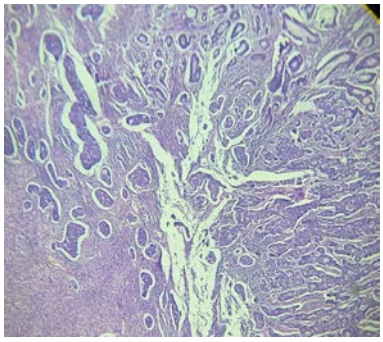


Image 5: Squamous Cell Carcinoma Cervix

6:



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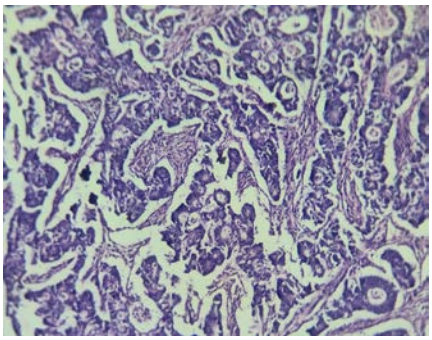

Image 6 and 7: Well Differentiated Endometrioid Adenocarcinoma FIGO Grade I

Postmenopausal bleeding is a very alarming sign that may be associated with cervical and uterine malignancies. The primary assessment in all cases of PMB should be trans-vaginal ultrasound scanning (TVS) as the thickening of endometrium may indicate significant pathology. The histopathology was recommended for only lesions with PMB when endometrial thickness is >4mm as measured by ultrasound.

In this present study majority of the biopsy specimens were received from cervix followed by endometrial curettage and hysterectomy specimen, our findings correlate with the Vidya[11] and Fatheha Ferdous[12].

Our results found that majority of the PMB constitute benign lesion on histopathological examination, in agreement with the Reyaz[13] and Ubeja[14]. Benign conditions included Atrophic Endometrium, Proliferative endometrium, Secretory endometrium, endometritis, endometrial polyp and endometrial hyperplasia without atypia.

PMB due to malignant and premalignant cases in present study was 47%, which is comparable with Naik[15] and Tyagi[16]. Among malignant condition Carcinoma in situ of cervix, endometrial hyperplasia with atypia and endometrial carcinoma were common Current study was noted that atrophic endometrium is the commonest among histopathological lesion in benign conditions, similar results are obtained by Karmarkar[17] and Kothapally[18]. The probable cause of PMB from atrophic endometrium are alteration of serum estrogen levels, degeneration of myometrial arterioles, chronic nonspecific endometritis, associated co morbidities like diabetes mellitus and hypertension, rupture of endometrial cysts and uterus prolapsed.

Studies done by Ahmed[19] and Damle[20] have been reported that the endometrial hyperplasia constitutes the commonest Histopathological organic lesion for postmenopausal bleeding. Endometrial hyperplasia is a most common predisposing factor and significant Histopathological condition that can lead to development of endometrial carcinoma.

In the present study it was noted that proliferative endometrium was the second most common cause of PMB which is comparable to study of Cheema[21].

Endometrial carcinoma is the most serious malignant lesion that can leads to postmenopausal bleeding, present study reported only 5.5% cases, similar to the study conducted by Sreelatha[22], whereas Irshaid[23] and Mallick[24] reported higher incidence of endometrial carcinoma were 9% and 9.3% respectively. This result may be probably due to high parity in our population group as endometrial carcinoma is more common in nulligravida.

Endometrial carcinoma is more associated with advancing age, late menopause thus this correlates with our study.

CONCLUSIONS

We have concluded that among benign causes Atrophic endometrium and proliferative endometrium were the significant cause of post-menopausal bleeding, whereas among the malignant causes, endometrial hyperplasia with atypia and Endometrial Carcinoma were most frequent histopathological findings. Therefore the study of endometrial histomorphology in PMB will help appropriate therapeutic management. A proper early diagnosis of PMB is immensely important for prompt treatment of patient by implementing a proper management plan can lead to reduces women mortality.

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