# Frequency of Endometrial Carcinoma in Patients with Postmenopausal Bleeding

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**Introduction:** Postmenopausal bleeding (PMB) is defined as bleeding that occurs after 1 year of amenorrhea in a woman who is not receiving hormone replacement therapy (HRT).[1] About 10% of women with postmenopausal bleeding have a primary or secondary malignancy. Common malignancies among them are endometrial cancer (80%), cervical cancer or an ovarian tumour.[1] Endometrial cancer is the second most common cancer associated with hereditary non-polyposis colorectal cancer.[2] Ninety percent of patients have benign causes.

**Objective:** The objective of this study was to determine the frequency of endometrial carcinoma in patients with post-menopausal bleeding.

**Study Design:** Descriptive case series study.

**Setting:** Department of obstetrics and gynaecology, Lady Willingdon, Lahore.

**Duration of Study:** This study was conducted over a period of six months from 1st January 2009 to 30th June 2009.

**Subjects and Methods:** 50 cases with postmenopausal bleeding.

**Results:** During the period of this study a total number of 50 consecutive patients who met inclusion criteria were enrolled in the study. Ages of the patients who presented with PMB ranged between 48 years and 80 years with a mean age of 59 years. Malignancy was found in 18 out of 50 cases (36%).Cases with endometrial CA were 14 out of 50 cases (28%) and CA cervix constituted 4 out of 50 cases (8%). Benign pathology was more frequent (64%). 13 of 50 cases (26%) had hyperplasia out of which 1 case (2%) was of atypical hyperplasia. Endometrial polyp was found in 4 of 50 cases (8%). 3 of 50 cases (6%) had chronic endometritis. 5 of 50 cases (10%) had chronic cervicitis. While 7 cases (14%) had postmenopausal bleeding due to decubitus ulcer of uterovaginal prolapse. Among malignancies (36%), endometrial cancer is the most frequent malignancy in women with postmenopausal bleeding with mean age of 65years.

**Conclusion:** In this study it was concluded that the majority of cases of PMB would be expected to be suffering from benign problems. The main aim of evaluation of cases of PMB is to exclude or identify endometrial or cervical carcinoma and atypical endometrial hyperplasia.

**Key Words:** Postmenopausal bleeding, menopause, endometrial carcinoma.

## Introduction

Postmenopausal bleeding (PMB) is defined as bleeding that occurs after 1 year of amenorrhea in a woman who is not receiving hormone replacement therapy (HRT).[1]

About 10% of women with postmenopausal bleeding have a primary or secondary malignancy. Common malignancies among them are endometrial cancer (80%), cervical cancer or an ovarian tumour.[1] Endometrial cancer is the second most common cancer associated with hereditary non-polyposis colorectal cancer.[2] Ninety percent of patients have benign causes; usually genital tract atrophy, polyps, endometrial hyperplasia, extra genital pathology, infections , medical disorder (e.g. cirrhosis of liver), decubitus ulcer in case of uterovaginal prolapse,[3] neglected porcelain pessary and forgotten IUCD.

Postmenopausal vaginal discharge, which may be blood stained or purulent is equally important like postmenopausal bleeding. Purulent vaginal discharge occurs in case of pyometra which is often seen in combination with endometrial cancer.[3]

The approximate age of menopause is 49 ± 3.6 years.[4] The proportion of women living to menopause and beyond has increased over the centuries with progressive increase in the life expectancy to approximately 82 years. As the women are spending increasing portion of their lives in menopause and thus postmenopausal problems are gaining more importance in gynaecological clinical practice.[5]

Postmenopausal bleeding is not a normal physiological phenomenon. Any bleeding should be considered abnormal in postmenopausal women except for those with predictable withdrawal bleeding taking hormone replacement therapy.[6] Sensitivity of transvaginal ultrasound in detecting endometrial pathology is 90 – 97%.[7]

As postmenopausal bleeding is the commonest symptom of endometrial carcinoma, so patients presenting with it should be worked up on priority basis for early detection and management of endometrial carcinoma.[8]

My study focused on the frequency of endometrial carcinoma which not only can help screening and diagnosis of postmenopausal bleeding but also its management at early stage.

## Aim and Objective

The objective of this study was to determine the frequency of endometrial carcinoma in patients with postmenopausal bleeding.

## Patients and Methods

This descriptive cross sectional study has been carried out on 50 women at Lady Willingdon hospital, Lahore from 1st Jan 2009 to 30th Jun 2009. All postmenopausal women presenting through emergency or outpatient department, with complaint of bleeding per vaginum, with their last menstrual period 1 year back and who were 45 years old or above, were considered eligible for participation after informed consent, irrespective of their parity, social background, previous medical, surgical or gynaecological history. Patients having premature menopause, surgical induced menopause, radiation induced menopause and chemotherapy induced menopause were excluded from the study. A full history of the patients was obtained. The name, age, parity, martial status (including husband name), address of the patients were noted. Details regarding vaginal bleeding were recorded. These included the timing of its onset, duration, colour and whether or not associated with passage of clots. History of associated symptoms included presence of any vaginal discharge, abdominal masses or distention, any accompanying abdominal pain or backache or a feeling of heaviness or something coming out of vagina. A history of recent weight loss or anorexia was noted as well as presence of any accompanying bowel or urinary symptoms. Treatments taken for the complaints were noted. Drug history especially that of hormone replacement therapy was also noted. Information regarding obstetrical history was obtained. Gynaecological history included details about age at menarche and menopause, menstrual cycle, contraceptive history coital history (also about post coital bleeding) and details regarding cervical smears was recorded. Past Medical and Surgical History was checked and questions regarding personal history were asked. A thorough general physical examination was performed with special attention to pallor, lymph nodes and breasts. Examination of the nervous system, cardiovascular system, respiratory system was performed in detail to look for any abnormal positive findings. Specific clinical examination including abdominal, speculum and bimanual pelvic examination was performed. Swabs were taken of any vaginal discharge and cervical smear was taken. Condition of the cervix and vaginal walls was noted. Bimanual examination was performed to assess the size, position and mobility of the uterus. Any adnexal heaviness was checked and presence of tenderness was noted. All patients had their blood group, haemoglobin, random blood sugar estimation, urine routine examination and coagulation profile. X-ray chest and ECG was performed as a requirement of the anaesthesia department for all patients. Pelvic ultrasonography from the Radiology Department was arranged. The size position and, contours of the uterus were assessed. Endometrial thickness was measured for every case. Patients were assessed by the anaesthetist and fitness for general anaesthesia was obtained. Examination under anaesthesia was performed. Fractional curettage was performed. Specimens from the cervix and endometrium were sent in different containers for histopathological examination to Pathology Department. Biopsy from any suspicious areas was taken. Endometrial polyps if present were avulsed and sent for histopathological examination. Addresses of the patients were carefully recorded so that they could be contacted.

## Results

During the period of this study a total number of 50 consecutive patients who met inclusion criteria were enrolled in the study. Ages of the patients who presented with PMB ranged between 48 years and 80 years with a mean age of 59 years. The maximum number of cases 14(28%) were between the ages 50 and 55 followed by 11(22%) patients between 56 and 60 years. Nine (18%) patients were between 45 – 50 years. While 6 (12%) patients were > 60 – 65 years. The age of 5 (10%) patients was between > 65 – 70 year. Three (6%) patients were between > 75 to 80 years of age. Only 2 (4%) patients were > 70 – 75 years (Table 1).

**Table 1:** *Frequency of Age of patients with PMB n = 50.*

| Ages in Years | No. of Patients | Percentage |
|---|---|---|
| 45 – 50 | 9 | 18 |
| > 50 – 55 | 14 | 28 |
| >55 – 60 | 11 | 22 |
| > 60 – 65 | 6 | 12 |
| > 65 – 70 | 5 | 10 |
| > 70 – 75 | 2 | 4 |
| > 75 – 80 | 3 | 6 |
| > 80 | 0 | 0 |

Age at Menarche of patients who presented with PMB ranged from 10 – 15 years. The maximum number of patients 20 (40%) had menarche at 12-13 years of age.

The current study reveals that age at menopause of the cases ranged from 45 years to 54 years. The maximum number of patients 20 (40%) had menopause at > 49 – 51 years. 13 (26%) patients had menopause at > 47 – 49 years. Twelve (24%) patients had menopause at > 51 – 53 years. Three (6%) patients had menopause at > 45 – 47 years while only 2 (4%) patients had menopause at > 53 – 55 years.

The period between menopause and onset of PMB ranged from 1 year to 32 years. The majority of patients 18 (36%) had > 5 – 10 years period between menopause and the onset of symptoms.

Parity of the cases ranged from $P_o$ to $P_9$ (mean parity 4.5). The majority of patients, 14 (28%) had parity of 3 – 4.

Patients presenting with PMB were divided into three groups according to the amount of vaginal bleeding. Bleeding was categorized as scanty if blood loss was less than that which occurs during normal menstruation. Moderate if it was similar to that which occurs during normal menstruation. Regarding the amount of per vaginal bleeding, majority 26 (52%) had scanty bleeding while 20 (40%) had presented with moderate bleeding and only 4 (8%) patients had severe per vaginal bleeding at presentation.

Along with PMB, the commonest associated symptom was vaginal discharge. Pain lower abdomen and low backache were the second most common associated symptoms.

Malignancy was found in 18 out of 50 cases (36%). Cases with endometrial CA were 14 out of 50 cases (28%) and CA cervix constituted 4 out of 50 cases (8%).

Benign pathology was more frequent (64%). 13 of 50 cases (26%) had hyperplasia out of which 1 case (2%) was of atypical hyperplasia. Endometrial polyp was found in 4 of 50 cases (8%). 3 of 50 cases (6%) had chronic endometritis. 5 of 50 cases (10%) had chronic cervicitis. While 7 cases (14%) had postmenopausal bleeding due to decubitus ulcer of uterovaginal prolapse (Table 2).

**Table 2:** *Histopathological Reports n = 50.*

| Histopathological Reports | | No. of Cases | Percentage |
|---|---|---|---|
| Hyperplasia | Simple | 10 | 20% |
| | Complex | 2 | 4% |
| | Atypical | 1 | 2% |
| Carcinoma | Endometrium | 14 | 28% |
| | Cervix | 4 | 8% |
| Benign Polyps | | 4 | 8% |
| Ulcer of uterovaginal prolapse | | 7 | 14% |
| Chronic Endometritis | | 3 | 6% |
| Chronic Cervicitis | | 5 | 10% |

Among malignancies (36%), endometrial cancer is the most frequent malignancy in women with postmenopausal bleeding with mean age of 65years. The youngest patient was 54 years old. While cervical cancer is the second most common malignancy with mean age of 60 years. The youngest patient was 50 years old.

## Discussion

Postmenopausal bleeding is frequent in gynecology and accounts approximately 3% of postmenopausal women.[8] This symptom can reveal benign causes as well as cancers. The primary aim is to identify and exclude atypical hyperplasia and endometrial carcinoma. The risk of endometrial carcinoma in women with postmenopausal bleeding rises with age from 1% at the age of 50 years to approximately 25% at the age of 80 years.[9]

In a recently conducted study, it was reported that postmenopausal women with vaginal bleeding have a probability of endometrial carcinoma of approximately 10%.[10] Shamsa Akhtar reported the incidence of endometrial cancer to be 19.4% in cases of PMB.[11] Here this probability was 27% (10 cases out of 36).

It has been reported[12] that the incidence of PMB decreases with increasing age. This study also proves the same. 25 (69.44%) cases of PMB were between 50 and 60 years of age, while only 5 cases (13.89%) were above 70 years of age.

The risk of malignancy of the endometrium is low in women under 50 years of age.[13] In this study all the 10 cases with endometrial carcinoma were between 60 and 80 years of age except 1 case that was 54 years of age.

Nulliparity, early menarche, chronic anovulation, late menopause, unopposed endogenous and exogenous oestrogens and Tamoxifen therapy have all been proven to be risk factors for the development of endometrial hyperplasia and carcinoma.[14] Here out of the total 10 cases of endometrial carcinoma 2 cases were nulliparous and also had early menarche (before 12 years of age), and 2 had late menopause (after 51 years of age).

Like wise obesity, diabetes mellitus and hypertension have been associated with endometrial carcinoma. In present study, out of the 10 cases mentioned above, 6 cases had BMI over 30.

Although, it has been reported in a rather old study that endometrial carcinoma is a disease of the upper socioeconomic group.[15] In this study, out of the 11 cases of atypical endometrial hyperplasia and endometrial cancer, only 2 belonged to the upper socioeconomic group, 5 to the middle and 4 to the lower socioeconomic group.

Endometrial hyperplasia is an oestrogen dependent condition and has the same risk factors as for endometrial carcinoma. The complex atypical hyperplasia has 25-30% incidence of progression to invasive carcinoma while simple hyperplasia has only 1% incidence of progression. Women with simple hyperplasia respond to hormonal treatment like levonorgestrol IUS[16] but with atypical hyperplasia should be offered total hysterectomy.[17] Bleeding with HRT users is more likely to be associated with benign pathology.[18] Tamoxifen therapy in the treatment or prevention of breast cancer increases the risk of endometrial cancer 3 – 6 fold.[19] The risk increases with higher doses and prolonged duration of Tamoxifen therapy.[20] All women with abnormal bleeding while taking Tamoxifen should be investigated to exclude malignancy.[21] Anastrozole (Arimidex) can be an alternative to Tamoxifen as it is associated with fewer episodes of postmenopausal bleeding.[22]

The assessment and investigations of cases of PMB is moving away from the operation theatre and ward

environment into the out patient department. The primary assessment in all cases of postmenopausal bleeding should be with transvaginal ultrasouns scanning (TVS), as the thickening of the endometrium may indicate the presence of significant pathology (e.g. endometrial cancer).[23]

Colour Doppler imaging in addition to TVS has not been found helpful in identification of endometrial pathology.[24] In this study I found that a normal ultrasound report in a woman with PMB was generally highly reassuring but histopathological examination of the endometrial tissue remained the mainstay for evaluation.

Endometrial screening using TVS on asymptomatic postmenopausal women often leads to unnecessary operations, increased morbidity and cost.[25] Saline sonohysterography is a useful diagnostic tool for identification of intrauterine polyps. Magnetic resonance imaging (MRI) is more accurate than transvaginal ultrasound in identification of site and size of primary tumour, extent of myometrial invasion and the presence of lymph node metastases but, it is expensive, time consuming and not suitable as a screening test for postmenopausal bleeding or depth of invasion.

Endometrial biopsy should be undertaken in all postmenopausal women with endometrial thickness (E.T.) greater than 4mm or persistent bleeding despite a normal E.T.[26] Dilatation and curettage is a blind procedure, it misses 10% of cases of endometrial lesions and samples only less than half of the endometrium in 60% of patients, so it should no longer be used as the first line method while evaluating the PMB.[27] Out – patient sampling with various devices like Pipelle and Vabra aspirators give equal diagnostic accuracy and lower complication rate although Pipelle causes less discomfort and samples less of the endometrial surface.[28] Procedure failure rate in out patient sampling is approximately 10%.[29] When comparing out patient sampling with hysteroscopy and curettage, both are equally effective in screening of endometrial hyperplasia but hysteroscopy is better at diagnosing benign lesions like polyp.[30] However, tissue biopsy is necessary with hysteroscopy for differentiation of premalignant and malignant endometrium.[31]

Present study proved fractional curettage as an essential investigation in the assessment of the endometrial status and also played an important role in the exclusion of local organic causes. This was consistent with the finding of the study by Noshin Wasim Yousaf.[32]

In this study fractional curettage was combined with cervical cytology and cervical biopsy in relevant cases. Fractional curettage is assuring for exclusion of carcinoma as the most women wanted to be 100% certain that carcinoma could be ruled out.[33]

## Comments

In this study it was concluded that the majority of cases of PMB would be expected to be suffering from benign problems. The main aim of evaluation of cases of PMB is to exclude or identify endometrial or cervical CA and atypical endometrial hyperplasia.

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