

Frequency of Endometrial Carcinoma in Patients with Postmenopausal Bleeding

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ABSTRACT

Objectives: To determine the frequency of endometrial carcinoma in patients with postmenopausal bleeding and to compare the clinico-demographic features of cases with and without carcinoma.

Study design: Descriptive study

Setting: Department of Obstetrics and Gynecology, Lahore

General Hospital affiliated with Postgraduate Medical Institute, from 14th April 2007 to 13th April 2008.

Materials and methods:

Sample: 100 patients of postmenopausal bleeding were included. Data was collected from history, examination, investigations and other relevant details of selected cases by using proforma questionnaire. Statistical analysis was done using software SPSS version 10.

Results: In present study, 7% cases were diagnosed as endometrial carcinoma on histopathology. All were endometrial adenocarcinoma. Most common cause of postmenopausal bleeding was atrophic endometrium (47% of cases) followed by endometrial hyperplasia, endometritis, endometrial and cervical polyps, cervical carcinoma and sub mucous fibroid, present in 19%, 13%, 8%, 4% and 2% respectively.

Mean age of patients with endometrial carcinoma was 69.28± 6.72 years and mean age of menopause was 53.14±3.76 years. Risk factors studied in patients with endometrial carcinoma, 15% had menopause after 55 years of age, 29% were nullipara, 43% patients were hypertensive, 29% were diabetic and 15% of patients had BMI more than 30Kg/m².

Conclusion: Study suggests that although the major causes of postmenopausal bleeding were found to be benign, the frequency of malignancy is still considerably high in women with postmenopausal bleeding in our population. This justifies the need for a thorough assessment and endometrial sampling in all cases of postmenopausal bleeding to decrease the morbidity and mortality associated with endometrial carcinoma.

Key words: Endometrial carcinoma, Postmenopausal bleeding

INTRODUCTION

Menopause, a natural step in aging process, is the permanent cessation of menstruation that results from loss of ovarian follicular activity. Natural menopause is recognized to have occurred after 12 consecutive months of amenorrhea for which there is no other obvious pathological or physiological cause. It occurs gradually in women and indicates the transition from the reproductive to the post productive era of a woman's life.¹ It is a condition that every woman faces in later life and can have many associated effects, which might disrupt the quality of life. Although the time spent in menopause (now up to one third of life cycle) has increased with phenomenon of increasing longevity, the actual age of menopause approximately 50-51year has not changed for centuries. The approximate age of menopause for white women is 51.4 years and for Asian women the mean age of menopause is 50.8years.²

Postmenopausal bleeding (PMB) is the bleeding that occurs after 1 year of amenorrhea in women who are not receiving hormone replacement therapy. It occurs in approximately 3% of postmenopausal women. Any bleeding should be considered abnormal in postmenopausal women except for those with predictable withdrawal bleeding taking hormone replacement therapy.³ However only 20% of patients with postmenopausal bleeding will have any significant pathology as a cause for their bleeding.³

Most of the patients have benign cause usually genital tract atrophy in 58.8%. Endometrial carcinoma in 9.4%, endometrial or cervical polyps in 9.4%, cervical carcinoma in 6%, sub mucous fibroid in 4% and 12.4% have endometrial hyperplasia, pyometra, ovarian cancer or urethral caruncle.⁴

Endometrial carcinoma is one of the common cancers of female genital tract. Women with relatively high levels of circulating oestrogens or

prolonged oestrogen influence are recognized high risk group for endometrial carcinoma.⁵ Risk factors for endometrial carcinoma include early menarche, late menopause, irregular bleeding, nulliparity, unopposed estrogen, obesity, diabetes mellitus, diet high in animal fat, tamoxifen use, personal and family history of breast, colon and endometrial malignancy.⁶

Now the women are spending increasing portion of their lives in menopause and thus postmenopausal problems are gaining more importance in gynaecological clinical practice. 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.⁷ Transvaginal ultrasound is a reliable test to screen the at risk population. Sensitivity of transvaginal ultrasonography in detecting endometrial pathology is 90-97%.^{8,9,10}

Endometrial carcinoma is one of the common cancers of female genital tract. It is also the most curable of gynaecological malignancies because it marks the presence at a stage when it can be cured by surgery alone.¹¹ Although literature show a lot of data on endometrial carcinoma in patients with postmenopausal bleeding but very few studies were conducted in our population so this study will add to the information about the frequency of endometrial cancer in patients with postmenopausal bleeding, and associated risk factors in our population. It will also help in the diagnosis of endometrial carcinoma and its management at early stage and thus to decrease the morbidity and mortality associated with endometrial cancer in our population.

METHODS

This study was conducted in the Department of Obstetrics and Gynecology Lahore General Hospital from 14th April 2007 to 13th April 2008(1 year) on 100 patients who presented with postmenopausal bleeding or blood stained vaginal discharge after 1 year of cessation of menses. Patients having premature menopause, surgical induced menopause, radiation induced menopause, chemotherapy induced menopause, with bleeding disorders, local trauma (vaginal pessary) and Patients taking hormone replacement therapy or anticoagulant drugs were excluded from the study.

Patients who fulfilled the inclusion criteria either presenting through emergency or outpatient

department were included in the study. Data was collected after an informed consent. Patients were diagnosed by detailed history and clinical examination. Pelvic ultrasonography, transvaginal scan, diagnostic dilatation and curettage carried out where indicated. Endometrial curettings were sent for histopathology, to pathology department. Patients were followed during hospital stay as well as in outpatient facility. Confounding variables such as delay in diagnosis, non availability of medicine and environmental conditions were controlled. All information was recorded on specially designed proforma.

Data analysis was computer based. Data entry sheet was designed in computer software SPSS version 10 and analyzed. Variables of interest include age, parity, age of menopause, presenting complaints etc. Quantitative variables such as age, age of menopause duration of bleeding, severity of bleeding would be analyzed using simple descriptive statistics like mean and standard deviation. Qualitative variables such as parity, presenting complaints, endometrial hyperplasia and endometrial carcinoma would be calculated using frequency and percentage and chi square analysis will be used as the data would be qualitative in nature.

RESULTS

During study period of 1 year there were hundred cases of postmenopausal bleeding, out of these 7 (7%) cases were diagnosed as endometrial carcinoma on histopathology. All were endometrial adenocarcinoma. Most common cause of PMB was atrophic endometrium in 47 (47%) of cases. Distribution of cases according to diagnosis is shown in Figure 1.

Mean age of patients was 61.7 ±6.70 years with a range from 53-80 years. Mean age of patients with endometrial carcinoma was 69.28± 6.72 years with a range from 60 years to 80 years while mean age of patients without endometrial carcinoma was 61.10 ±5.89 years with a range from 53 years to 80 years.

In current study, Mean parity was 5.81±2.11 with a range from nullipara to para 11. Mean parity of patients with endometrial carcinoma was 2.85±2.34 with a range from nullipara to para 6. The cases without endometrial carcinoma had a mean parity 5.94±1.9 with a range from nullipara to para 11. Results showed that women with low parity have a higher risk of endometrial carcinoma.

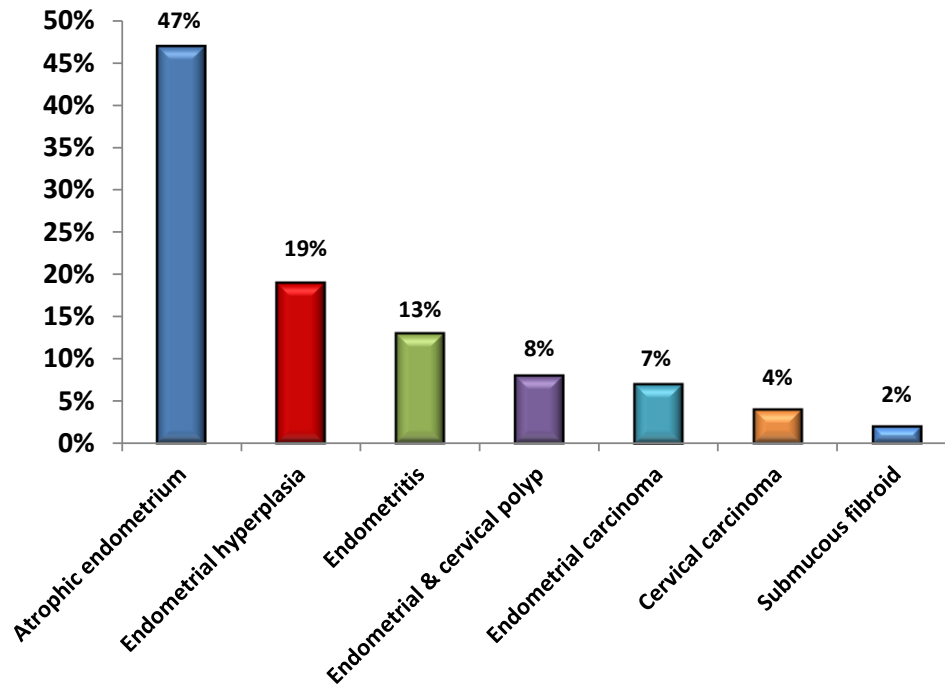


Figure 1: Distribution of cases according to diagnosis

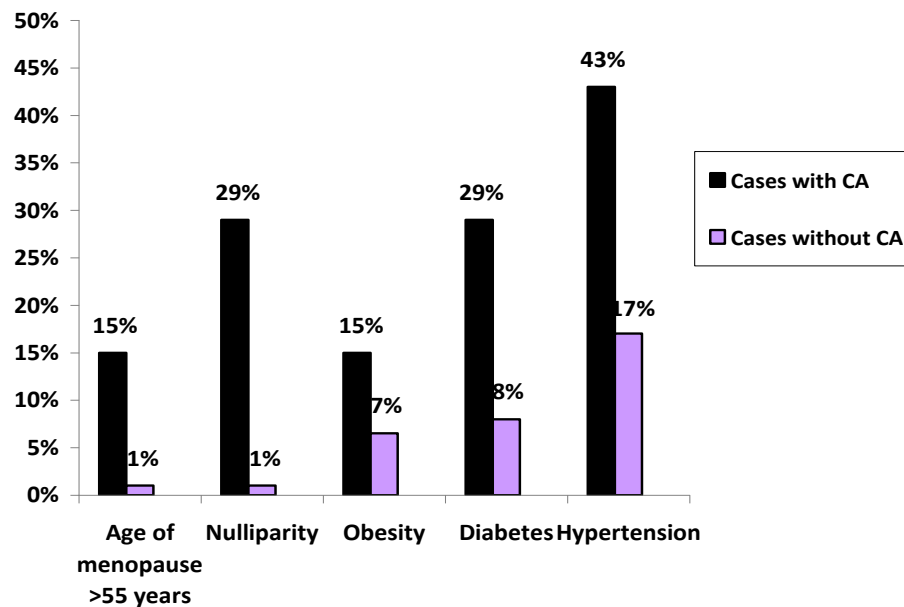


Figure 2: Comparison of clinico-demographic features of cases with and without endometrial carcinoma

Age of menopause was studied in 100 patients and mean age of menopause was 49.6 ± 2.73 years with a range from 45 years to 60 years. Mean age of menopause was 53.14 ± 3.76 years with a range from 50-60 years in patients with endometrial carcinoma. On the other hand cases without endometrial carcinoma had mean age of menopause 49.50 ± 2.70 years with a range from 45 years to 60 years.

Transvaginal ultrasound was done for endometrial thickness.

The patients with endometrial carcinoma had mean endometrial thickness 13.71 ± 3.09 mm.

All patients included in the study were assessed for risk factors of endometrial carcinoma like age of menopause, nulliparity, obesity, hypertension, diabetes mellitus, personal and family history of malignancy as shown in Figure 2.

Anorexia was present in 71.4% patients with endometrial carcinoma as compare to 19.4% without endometrial carcinoma. Weight loss was present in 42.9% cases with carcinoma as compare to 11.8% cases without carcinoma. Out of 7 cases with endometrial carcinoma family history of malignancy was present in 28.6% patients as compare to 7.5% patients without endometrial carcinoma. Out of 7 patients of endometrial carcinoma, 14.3% patient had personal history of malignancy in comparison to 3.2% patients without carcinoma.

DISCUSSION

Postmenopausal bleeding accounts for a significant proportion of gynecological referrals and occurs in approximately 3% of postmenopausal women. Benign causes represent the most frequent cause of PMB and can cause considerable distress. The primary aim of initial investigations is to exclude endometrial carcinoma and atypical endometrial hyperplasia.

In current study 7 (7%) cases were diagnosed as endometrial carcinoma on histopathology. All were endometrial adenocarcinoma. Findings are comparable to the study of Sarfraz T et al which showed endometrial carcinoma in 6% case.¹²

Most common cause of PMB was atrophic endometrium in 47 (47%) cases which is consistent to the study of Asim SS et al which showed atrophic endometrium in 50% cases.¹³ Results of current study are different from the study of Fernando MS et al in which endometrial atrophy was present in 29.4% of cases.¹⁴ The

second common cause of PMB in this study was endometrial hyperplasia in 19 (19%) cases. In present study 12% cases were of simple cystic hyperplasia, 5% cases of complex endometrial hyperplasia without atypia and 2% cases of complex endometrial hyperplasia with atypia. The results of this study are comparable to the study of Sarfraz T et al, in which simple cystic hyperplasia was present in 17% cases, glandular hyperplasia without atypia in 6% and with atypia in 4% cases.¹² In current study endometritis was found in 13 (13%) cases which are consistent to the study of Sarfraz S et al which showed 11% endometritis,¹² while the study of Fernando MS et al showed endometritis in 5.8% cases.¹⁴

Endometrial and cervical polyps were present in 8 (8%) patients that are comparable to study of Gredmark T et al which showed uterine polyps in 9% cases.¹⁵

Cervical carcinoma contributed to 4% cases of PMB, which is comparable to O'Gorman T et al which shows cervical carcinoma in 6% cases⁴ and Ghazi A et al, according to which carcinoma of cervix was present in 8.8% cases.¹⁶ The results of current study are in contrast to the study of Ergete W et al which is a retrospective analysis of four years biopsy from 475 women with PMB which showed cervical carcinoma in 51.6% cases. The reason for this high rate of cervical malignancy as a cause of postmenopausal bleeding might be the lack of awareness and accessibility for modern health care, high prevalence of human papilloma virus and inefficient use of screening methods such as pap smear for detection of precursor lesions of cervical cancer.¹⁷ 2 (2%) patients had sub mucous fibroid which is comparable to the study of Gredmark T et al according to which 4% of patients with PMB had sub mucous fibroid.¹⁵

I assessed all of my patients for risk factors of endometrial carcinoma like age of menopause, nulliparity, obesity, hypertension, diabetes mellitus, personal and family history of malignancy. In current study, mean age of patients with endometrial carcinoma was 69.28 ± 6.72 years while mean age of patients without endometrial carcinoma was 61.10 ± 5.89 years. 15% of patients with endometrial carcinoma had age of menopause more than 55 years while 1% patients without CA [Figure 2] and a study conducted by Gredmark T et al showed 25% risk at 80 years of age.¹⁵

29% of patients with endometrial CA were nullipara as compare to 1% of patients without CA [Figure 2]. The study of Anne M et al showed that parity was related inversely (odds ratio 0.70, $p=0.002$) to the risk of endometrial neoplasia.¹⁸

The age of menopause in current study is 49.6 ± 2.73 years which is consistent to the study by Yahya S et al and Qazi RA.^{19, 20} Cases diagnosed as endometrial carcinoma had delayed menopause (age >55 years) in 15% cases as compared to 1% of cases without carcinoma [Figure 2].

The patients with endometrial carcinoma had mean endometrial thickness 13.71 ± 3.09 mm. These findings are consistent to the study of Bruchim I et al according to which mean endometrial thickness was 13.5 ± 7.7 mm in patients with endometrial carcinoma.²¹

Blood pressure of all patients, included in the study was measured and results showed that 43% of patients with endometrial carcinoma were hypertensive while 17% patients were hypertensive in cases without endometrial carcinoma [Figure 2]. The study by Anne M et al showed hypertension as one of the risk factor for endometrial carcinoma in patients with PMB.¹⁸

The results of current study showed that 29% patients with endometrial carcinoma had diabetes mellitus as compare to 8% cases without CA. A case control study conducted by Anne M et al showed that diabetes (odds ratio 3.5, $p=0.52$) was marginally significant factor associated with endometrial carcinoma.¹⁸

In present study, 15% of patients with endometrial CA had BMI more than 30Kg/m^2 while 7% were obese in cases without CA. This showed that higher values of BMI were found in cases with endometrial carcinoma. The results are comparable to the study of Anne M et al, according to which obesity is directly related to the risk of endometrial carcinoma (odds ratio 1.02 per Kg, $p=0.018$). A prospective case control study by Gredmark T et al showed that BMI was higher in postmenopausal women with endometrial adenomatous and atypical hyperplasia.¹⁵

Results of the study showed that although senile endometrial atrophy was most commonly found in patients with PMB but a significant percentage of endometrial hyperplasia and endometrial cancer implies the need for investigating all cases of postmenopausal bleeding. Bimanual examination and pelvic ultrasonography should be combined with

endometrial sampling so such rare pelvic pathologies may not be missed.

CONCLUSION

The study shows benign conditions represent the most frequent causes of postmenopausal bleeding though primary aim of initial investigations is to exclude endometrial carcinoma and atypical hyperplasia.

The study also showed that frequency of malignancy increases with an increasing age, late age at menopause, nulliparity, obesity, diabetes mellitus, and hypertension.

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