

POSTMENOPAUSAL BLEEDING-AN ALARMING SYMPTOM OF ENDOMETRIAL CARCINOMA

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ABSTRACT

Objective: To investigate the clinical significance of postmenopausal bleeding in terms of risk factors, incidence of endometrial carcinoma and histopathological evaluation of endometrium.

Material and Methods: This descriptive study was carried out in Obstetrics and Gynaecology Unit "C", Khyber Teaching Hospital, Peshawar, from January 2012 to February 2014. A total of 36 patients with postmenopausal bleeding were enrolled in the study (aged 49-78 years). These patients were evaluated by transvaginal ultrasonography, diagnostic curettage and endometrial biopsy followed by histological assessment of the endometrium.

Results: On histological analysis, malignancy was found in 33.3% cases. The most common malignancy was endometrial carcinoma (30.55%), while one case of cervical carcinoma (2.8%) was detected. Pre-malignant lesions (atypical endometrial hyperplasia) were found in 14% cases. Benign causes were responsible for 52.8% cases of postmenopausal bleeding, among them atrophic endometrium was the most common finding (36.8%), followed by chronic endometritis (31.6%) and benign endometrial polyps (26.3%). Furthermore, obesity (72.7%), diabetes mellitus (54.5%) and hypertension (27.3%) were frequently observed in patients with endometrial carcinoma.

Conclusion: Postmenopausal bleeding is an alarming symptom and therefore, further investigation is mandatory in order to detect endometrial cancer at an early stage and affect a cure.

Key Words: Postmenopausal, bleeding, Transvaginal scan, endometrial carcinoma.

INTRODUCTION

World Health Organization (WHO) defines menopause as permanent cessation of menstruation, resulting from loss of ovarian activity¹. Postmenopausal bleeding (PMB) is defined as bleeding that occurs from the genital tract more than 12 months after the last menstrual period in a woman who is not receiving hormone replacement therapy². Post menopausal bleeding represents one of the most common reasons for referral to gynecological services, mainly due to the suspicion of an underlying endometrial malignancy³, as approximately 90% of women with endometrial carcinoma presents with postmenopausal bleeding as the only presenting complaint⁴.

A woman not taking hormone replacement therapy that bleeds after the menopause has a 10%-15% risk of having endometrial carcinoma. Furthermore, endometrial cancer is the most common gynecological malignancy in the United States. Annually; there are approximately 46,470 new cases and 8,120 deaths from the disease⁵.

About 80-90% of patients presenting with postmenopausal bleeding have benign causes; usually atrophic vaginitis, endometrial or cervical polyps, simple endometrial hyperplasia, infections, medical disorders (e.g., cirrhosis of liver), decubitus ulcer in cases of uterovaginal prolapse, neglected pessary and forgotten intra uterine contraceptive device⁶. However, more sinister causes of the bleeding such as atypical endometrial hyperplasia and endometrial carcinoma must first be ruled out. Patients at risk of endometrial carcinoma are those who are obese, diabetic and/or hypertensive, nulliparous, taking exogenous estrogens (including tamoxifen) or those who experience late menopause⁷.

Transvaginal ultrasonography (TVS) is the recommended first line, non invasive procedure for assessing the endometrium in women with postmenopausal bleeding. Measurement of endometrial thickness by TVS having a cut off of > 4mm yields 98% sensitivity for detection of endometrial carcinoma⁷.

Dilatation and curettage and hysteroscopic guided endometrial biopsy are valuable tools to evaluate the underlying etiology of post menopausal bleeding. Post menopausal bleeding is not a physiological phenomenon, so any bleeding should be considered

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abnormal in postmenopausal women except for those with predictable withdrawal bleeding taking hormone replacement therapy⁸.

As post menopausal bleeding is the commonest symptom of endometrial carcinoma, hence patients presenting with it should be worked up on priority basis for early detection and management of endometrial carcinoma⁹. Therefore, this study was conducted to present a hospital based survey, to determine the clinical significance of postmenopausal bleeding in terms of risk factors, incidence of malignancy and histopathological evaluation of causes of postmenopausal bleeding.

MATERIAL AND METHODS

This descriptive study was carried out on 36 patients at Obstetrics and Gynaecology Unit C, Khyber Teaching Hospital, Peshawar from January 2012 to February 2014. Postmenopausal women who presented clinically with complaint of vaginal bleeding, with their last menstrual period at least one year back and who were 45 years old or above were considered eligible for participation after taking informed consent. Approval of the study was taken from hospital's ethical committee.

Patients having pre-mature menopause, surgical induced menopause, radiation induced menopause and chemotherapy induced menopause were excluded from the study. Detailed history was obtained from the patients including name, age, marital status, parity and postal address.

Details regarding vaginal bleeding were recorded. These included the timing of onset, duration and amount of bleeding. History of associated symptoms including presence of vaginal discharge, abdominal mass or pain and history of recent weight loss was obtained. Drug history especially, that of anticoagulants, hormones replacement therapy and tamoxifen therapy was also noted. Past medical and surgical history was checked especially regarding hypertension, diabetes mellitus and liver diseases.

A thorough general physical examination was performed. Height and weight of the cases measured and body mass index (BMI) calculated. Blood pressure was recorded. Specific clinical examination including abdominal, speculum and bimanual pelvic examinations were performed to assess the cervix and to determine size, position and mobility of the uterus. Cervical smears were taken.

All base line investigations including Full blood count, Random blood sugar, Urine routine examination, Coagulation profile, X- ray chest and ECG were requested. In all patients Transvaginal ultrasonography (TVS) from the radiology department was arranged. The

size, position and contour of the uterus were assessed. Endometrial thickness (double layered) measured and recorded in all cases.

Opinion regarding fitness for anesthesia was obtained from the anesthetist. After taking written informed consent Examination under anesthesia (EUA), cervical smear and dilatation and curettage (D &C) were performed. Endometrial polyps, if found were avulsed. The specimens were collected in separate containers and sent for histopathological examination to pathology department. The data was entered into SPSS version 10 and results were obtained.

RESULTS

The mean age of women with postmenopausal bleeding (PMB) was 58.2 years (range 49-78). The period between menopause and onset of PMB ranged from one year to 27 years. Age distribution of women with postmenopausal bleeding is shown in Table 1. However, the majority of patients (66.7%) had < 10 years time period between menopause and the onset of symptoms of postmenopausal bleeding. Hence, the incidence of postmenopausal bleeding declined with increasing age. Furthermore, it was noticed that the incidence of malignancy increased with increasing time period between menopause and onset of postmenopausal bleeding. In 9(81.8%) cases with endometrial carcinoma as a cause of postmenopausal bleeding, had ages between 61-70

Table 1: Age distribution of cases with postmenopausal bleeding

Age in years	Cases and percentage
49-51	5(13.8%)
52-60	19(52.77%)
61-70	9(25%)
>70	3(8.3%)

Table 2: Histopathological findings of endometrium

Histopathological findings of endometrium	Cases and percentage
Benign causes	
Atrophic endometrium	7(36.8%)
Chronic endometritis	6(31.6%)
Benign endometrial polyps	5(26.3%)
Proliferative endometrium	1(5.3%)
Premalignant causes	
Atypical Endometrial hyperplasia	5(14%)
Endometrial carcinoma	11(30.55%)
Cervical carcinoma	1(2.8%)

years (mean age 67.5 years).

The majority of the patients (75%) had parity of > P4. The histopathological findings of endometrium in patients with postmenopausal bleeding are shown in Table 2. The most common subtype of endometrial carcinoma was endometrioid carcinoma (81.8%) followed by papillary serous carcinoma (18.2%).

It was noted, that most patients presented with multiple medical co-morbidities with common associations of obesity, diabetes mellitus type-2 and hypertension. The most frequently observed risk factor in cases of endometrial carcinoma was obesity (72.7%) followed by diabetes mellitus and hypertension.

Only one case (2.7%) has been diagnosed as having carcinoma cervix (squamous cell carcinoma) as the cause of PMB. It was found that (90.9%) patients who had been diagnosed as having endometrial carcinoma had endometrial thickness of > 4mm on transvaginal ultrasonography.

DISCUSSION

Postmenopausal bleeding is common between 5-10 years after reaching menopause and is most common between 50-60 years of age¹⁰. Our study also confirms this finding as (66.7%) cases in our study presented between 49-60 years with symptom of postmenopausal bleeding. However, the peak incidence of endometrial carcinoma was observed in the age group of 60-70 years (mean 67.5 years). This result is in accordance with several recent studies^{11,12}. In our study most of the patients (75%) were multiparous (parity > 4). Previous studies have shown that the risk of endometrial carcinoma is inversely related to parity¹³. Nulliparity, however by itself does not appear to increase the risk; instead, the association probably lies with the high frequency of anovulatory cycles in infertile women^{14,15}. However, a recent study conducted in India showed that most of the women presented with postmenopausal bleeding were multiparous¹⁰.

In the present study, genital tract malignancies were found in (33.33%) cases. Studies conducted in different parts of Pakistan showed incidence of genital tract malignancies of 20-53.7%^{16,17,18}. However, our findings are in contrast with studies carried out in the developed countries where the reported figures are between 9.9-11%^{19,20,21}. The relatively high incidence of malignancies in our part of the world reflects the lack of education, un-awareness of women regarding health issues and non availability of screening facilities²².

In our study, Endometrial carcinoma accounted for 30.5% cases of postmenopausal bleeding. A study conducted by Yousaf S et al⁹, in Lady Willingdon Hos-

pital, Lahore, showed similar results. However, relatively lower incidence of Endometrial carcinoma in PMB patients has been shown by Jillani K et al³ (16%) and Ghazi et al¹⁸ (11.1%) which showed carcinoma cervix as the most common malignancy in PMB patients.

Pre malignant lesions such as atypical endometrial hyperplasia was found in (26.3%) cases. Previous studies have revealed that the presence of atypical endometrial hyperplasia is a worrisome feature as approximately 20-25% of such cases with atypia will have a concomitant endometrial carcinoma and/or may develop carcinoma if left untreated². The most common histological subtype of endometrial carcinoma was Endometrioid carcinoma (81.8%) followed by Papillary Serous carcinoma. This result is in agreement with previous reports^{23,24}.

In this study the most common benign histopathology of endometrium was atrophic endometrium (36.8%) followed by chronic endometritis (31.6%). These findings have also been observed in previous studies^{2,10,25}. One possible explanation for this atrophic endometrium and endometritis in postmenopausal bleeding is the fragile vascular support provided by thin underlying stroma resulting in superficial petechial hemorrhages and mucosal ulceration and probably superimposed infection¹³.

In our study benign endometrial polyps were responsible as a cause of postmenopausal bleeding in (26.3%) cases. Similar result has been shown by Banfa et al²⁶. Polyps are actually friable vascular network which may rarely contain foci of hyperplasia or cancer¹³.

Interestingly, in our study an association between Obesity (BMI > 29 kg/m²), Diabetes Mellitus type-2 and Hypertension has been observed in patients with endometrial malignancy. The most frequently observed medical co-morbidity was obesity as (72.7%) of the patients diagnosed as having carcinoma endometrium were obese (BMI > 29kg/m²). Several previous studies have confirmed the strong association between obesity and carcinoma endometrium^{27,28}. One explanation for this association is that obese women have high levels of endogenous estrogens due to conversion of androstenedione to estrone and the aromatization of androgens to estradiol, both of which occur in peripheral adipose tissue^{29,30}. Furthermore, obese women can also have lower circulating levels of sex hormone binding globulins, alterations in the concentration of insulin like growth factor and its binding proteins, and insulin resistance all of which may contribute to the increased risk of endometrial carcinoma in these women³¹.

In our study, out of 11 cases diagnosed as having endometrial carcinoma (54.5%) were known type

2 diabetics. While (27.3%) were hypertensive. Several recent studies have also shown that women with type 2 diabetes mellitus and hypertension are at increased risk of endometrial carcinoma^{32,33,34,35,36}. Diets high in carbohydrates and associated hyperinsulinemia, insulin resistance and elevated levels of insulin like growth factor may play a role in endometrial proliferation and development of endometrial carcinoma^{33,37,38}.

Several large multi- center studies have reported a high sensitivity of transvaginal scan (96-98%) in identifying postmenopausal women at risk of endometrial carcinoma^{39,40}. Our result (90.9%) is in agreement with the previous reports. Though we found that a normal ultrasound report (endometrial thickness of < 4mm) in a woman with postmenopausal bleeding was highly reassuring but histopathological examination of the endometrium remained the main stay of evaluation.

CONCLUSION

Postmenopausal bleeding should always be taken seriously and investigated meticulously no matter how minimal or insignificant it may appear.

Recommendation

Transvaginal ultrasonography (TVS) should be the first-line investigation in postmenopausal women with bleeding. An endometrial thickness of > 4mm measured by TVS should be further evaluated by endometrial biopsy on priority basis in order to exclude endometrial carcinoma and/or atypical endometrial hyperplasia.

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