POSTMENOPAUSAL BLEEDING - A STRONG INDICATOR OF ENDOMETRIAL CARCINOMA

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ABSTRACT

Objective: To determine the demographic profile, patterns of bleeding and histopathological patterns of endometrial biopsy in women presenting with postmenopausal bleeding.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Gynaecology and Obstetrics Department, MTI/Mardan Medical Complex, Mardan Pakistan, from Apr 2016 to Mar 2017.

Material and Methods: This descriptive cross sectional study was included women of any parity and age >45 years who had spontaneous cessation of menstruation for the last one year while premenopausal women, drug or irradiation induced or iatrogenic menopause were excluded. All patients were admitted, transvaginal ultrasound done (cut off endometrial thickness >4mm) and subjected to dilatation and curettage under anesthesia and endometrial biopsies obtained. Samples were sent for histopathology and followed.

Results: A total of 35 women were included. Commonest age group was 61-70 years, and was seen in 19 (54.3%) women, followed by 52-60 years age group where 9 (25.7%) subjects were observed. Mean age was 62 ± 2.54 years. Twelve (35%) women were hypertensive while Type 2 Diabetes Mellitus (T2DM) was seen in 7 (20%). Twenty (57%) women complained of streak of blood on sanitary pad, and in 28 (80%) there were recurrent episodes. Twenty four (68.57%) women were multiparous. Atrophic endometrium was the most common benign histopathological pattern, seen in 9 (26%) followed by 8 (23%) chronic endometritis. Endometrial carcinoma was seen in 8 (23%) subjects with endometroid carcinoma in 28 (80%) cases.

Conclusion: Postmenopausal bleeding is an alarming symptom and should be thoroughly investigated with transvaginal ultrasound followed by endometrial biopsy for timely diagnosis and treatment.

Keywords: Atrophic endometrium, Endometrial carcinoma, Postmenopausal bleeding, Transvaginal ultrasound.

INTRODUCTION

Menopause is defined as the last menstrual period after a minimum of one year's amenorrhoea[1]. There is no mutual consensus for deciding the appropriate interval of amenorrhoea which will precede an episode of vaginal bleeding due to the anovulatory cycles that precedes menopause[2]. It is estimated that 1-25% and on the average 10% women who present to the clinicians with postmenopausal bleeding will be ultimately diagnosed with endometrial carcinoma. Endometrial atrophy is the most common cause amongst the postmenopausal women. Endometrial polyps and hyperplasia are other common causes[3].

In the US, endometrial cancer is the most commonly diagnosed reproductive tract malignancy and is the fourth most common cancer among women, superseded by cancers of breast, lung and colorectal origin. Although it is responsible for causation of 6% of female malignancies, its ease of diagnosis and timely therapy makes it responsible for only 3% of malignancy related deaths[4]. There are two types of endometrial carcinomas, type I is secondary to unopposed estrogen induced endometrial hyperplasia and type II are serous or clear cell origin, are independent of estrogen stimulation and have relatively poor prognosis[5]. Recent data shows that type I comprises 90% and type II comprises 10% of endometrial malignancies[6].

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For women receiving hormone replacement therapy, the pattern of bleeding depends on the type of gonadal steroids, especially the progestogens. Break through bleeding occurs in women taking estrogen alone or both estrogen and progestogens. Fifty percent of women on hormone replacement therapy (HRT) experience breakthrough bleeding. In women with uterus, systemic estrogens of HRT increase the risk of endometrial carcinomas, even after its use is stopped. For postmenopausal women not taking HRT, risk of endometrial carcinoma is 4.9% to 11.5%[7].

Risk factors for endometrial carcinoma are obesity, hypertension and hyperestrogenism (exogenous or endogenous)[8]. Early menarche, late menopause and nulliparity due to high frequency of anovulatory cycles is also a risk factor. Hereditary non polyposis colorectal cancer is a rare risk factor with relatives of an affected family member having 50% risk of endometrial cancer[9].

Transvaginal ultrasonography is used to measure thickness of endometrium. This should be thinner in post menopausal women (<4mm) not receiving HRT. This is by convention a double thickness in mid sagittal view called Endometrial Echo Complex (EEC)[10]. In general, thicker EECs are associated with a greater risk of endometrial lesions. Sampling of endometrium can be accomplished by devices for office use like pipelle, suction catheter, by dilatation and curettage, or under hysteroscopic guidance. Any method of sampling the endometrium will certainly miss a proportion of endometrial carcinoma[11].

The aim of our study is to conduct a hospital based survey to determining the risk factors for endometrial carcinoma, its incidence and histopathological assessment.

PATIENTS AND METHODS

This descriptive cross sectional study was conducted at Gynaecology and Obstetrics Department of Mardan Medical Complex, from April 2016 to March 2017. All postmenopausal women irrespective of parity, who presented with vaginal bleeding of any amount, were included in the study. Menopause was considered a period of spontaneous amenorrhoea of one year time period. Premenopausal women, those having premature menopause, iatrogenic menopause, irradiation or drug induced menopause or with incidental finding of increased endometrial thickness on ultrasound were excluded from the study. Sample size was calculated by using WHO sample size calculator and non-probability convenience sampling technique was adopted for this study.

Approval from hospital ethical committee was obtained. Written informed consent was taken from all patients after explaining them the purpose of study. Patients were recruited from outpatient department (OPD), detailed history was taken regarding age, parity, time since menopause, number of episodes of vaginal bleeding whether single or recurrent, amount of bleeding whether spotting, streak of blood on sanitary pad or fully soaked pad. Associated vaginal discharge, abdominal mass or history of weight gain or loss was also inquired. Drug history with special emphasis on intake of anticoagulants or antiplatelets, Tamoxifen and HRT was also taken. Diabetes, hypertension and any hepatic disorders were recorded as part of past medical history.

Thorough general physical examination including body mass index and blood pressure was recorded. Abdominal, bimanual pelvic and speculum examination was performed to evaluate uterus and cervix and smears obtained. Baseline investigations, bleeding and clotting profile, ECG and chest x-ray were performed from hospital laboratory and radiology department. Transvaginal ultrasound was done to evaluate uterus for endometrial thickness with cut off at 4mm. Anesthesia fitness was confirmed from anesthetist and examination under anesthesia (EUA) was done after written informed consent. Dilatation and curettage was performed. Specimens were sent for histo-pathology. Patients discharged on the same day.

Her histopathology reports and cervical smear results were followed in the OPD.

Data collected and analyzed in SPSS version 20.0. Mean and standard deviation calculated for numerical data and frequencies and percentages calculated for categorical variables. All data presented in the form of tables.

RESULTS

A total of 35 women were recruited into the study. Four age groups were created and subjects allocated into each group. Five (14%) subjects were between 45-51 years age, 9 (25.7%) women were 52-60 years age, 19 (54.3%) were 61-70 years and 2 (5.7%) were more than 70 years age. Mean age was 62 ± 2.54 years.

Seven (20%) women had diabetes and 12 (35%) were hypertensive. Eleven (31.4%) women were nulliparous and 24 (68.57%) were multiparous (table-I).

Twenty (57%) women complained of a streak of blood on pad when asked about the amount of bleeding. Eight (23%) said it was mere spotting and in case of 7 (20%), it was heavy bleeding with soaking of full sanitary pad. Seven (20%) subjects had a single episode of per vaginal bleeding and 28 (80%) had this complaint for multiple times before they sought medical advice (table-II).

Amongst the etiology, benign causes were more common when histopathological reports were reviewed. Atrophic endometrium was the most common, being seen in 9 (26%) subjects,

Table-I: Demographic characteristics (n=35).

Demographic variable		Frequency	Percentage
Age	45- 51 years	5	14
	52- 60 years	9	25.7
	61- 70 years	19	54.3
	>70 years	2	5.7
Parity	Nulliparous	11	31.4
	Multiparous	24	68.57
Diabetes	Yes	7	20
	No	28	80
Hypertension	Yes	12	34
	No	23	66

Table-II: Patterns of postmenopausal bleeding (n=35).

	Frequency	Percentage
Spotting	8	23
Light	20	57
Heavy	7	20
Frequency of Bleeding		
Single Episode	7	20
Recurrent Episodes	28	80

Table-III: Etiology of postmenopausal bleeding on the basis of histopathological reports (n=35).

Histopathological Report	Frequency	Percentage
Benign Disorders		
Atrophic Endometrium	9	26
Chronic Endometritis	8	23
Polyps	4	11.4
Proliferative Endometrium	1	2.8
Premalignant/Malignant Disorders		
Endometrial Carcinoma	8	23
Atypical Endometrial Hyperplasia	5	14
Cervical Carcinoma	1	2.8

followed by chronic endometritis in 8 (23%), polyp in 4 (11.4%) and proliferative endometrium in 1 (2.8%) cases. Amongst the premalignant and malignant etiologies, endometrial carcinoma was seen in 8 (23%), atypical endometrial hyperplasia in 5 (14%) and cervical carcinoma was seen in 1 (2.8%) case of postmenopausal bleeding. Commonest type of endometrial carcinoma seen was endometroid carcinoma seen in 28 (80%) subjects (table-III).

In our study, 22 (63%) subjects had time period of less than 10 years between menopause and initiation of postmenopausal bleeding, but the risk of malignancy increased with increasing interval between menopause and development of symptoms.

DISCUSSION

The main objective in managing a patient with postmenopausal bleeding is to exclude malignancy. Although 80-90% of patients presenting with this complaint had benign etiology, premalignant and malignant causes must be ruled out.

The commonest age group seen in our study was 61-70 years age, with mean age being 62 ± 2.54 years. Our result correlates with the study done by Burbos *et al* where the mean age was 64 years[12] and the studies done by Davis *et al* by Von Doorn *et al* in terms of common age group[12-14]. Regarding parity, 68.57% of our patients were multiparous. Nulliparity has been considered to be a risk factor for endometrial carcinoma not because of tself but due to the anovulatory cycles in infertile subjects. In a study done by Kothapally *et al* at Andhra Pradesh, India, it was concluded that most of the women with postmenopausal bleeding with ultimate histopathological findings of endometrial carcinoma were multiparous[15].

Diabetes was co-morbidity in 20% of our studied population. Burbos *et al* reported the figure around 17%[12] and Visser *et al* reported it as 12.9%[16], whereas it was present in 54.5% of women studied by Fatima *et al* at Khyber Teaching Hospital, Peshawar[17]. Food with high carbohydrate contents, hyper insulinemia, resistance to insulin and high levels of insulin like growth factors are related to division of endometrial cells thus leading to endometrial carcinoma[18]. Hypertension was seen in 35% cases in our study. This is in accordance with different national and international studies where figures of 34.4% and 27.3% were seen[16,17,19].

Most of our patients (57%) presented with a light episode of vaginal bleeding. This much amount of bleeding was reported by 55% of subjects in a study done at Norwich, UK in 2010[12], whereas frequency were reported as recurrent in the same study in 76% cases, close to our study (80%).

Regarding the histopathological reports of these patients, we observed that 26% of our cases had atrophic endometrium, followed by chronic endometritis in 23% cases. Similar findings have been reported by different authors in their studies[15,20,21]. The reason might be that the very weak and fragile support of blood vessels which is provided by stromal tissue leads to hemorrhages and ulcerations in mucosal lining and may also lead to infection (endometritis)[22]. Polyps were seen in 11.4% cases in our study, which is in contrast to the study by Fatima *et al* where they reported 26% cases of postmenopausal bleeding due to polyps[17]. Banfa *et al* reported close figures to ours whereas it was high in a study conducted by Ghoubara *et al* in 2018[23,24].

In the premalignant and malignant etiologies, atypical endometrial hyperplasia was seen in 14% cases. Brand *et al* reported similar results and it has been suggested that atypical endometrial hyperplasia is indeed a trouble some finding as it precedes the development of endometrial carcinoma or may be harboring it at that time[20]. Endometrial carcinoma was seen in 23% of our study population, whereas it was responsible for causation of postmenopausal bleeding in 16% subjects in the study conducted by Jillani *et al* and 11% in study conducted by Ghazi *et al*[25,26]. These are relatively lower figures as compared to ours. Yousaf *et al* in their study at

Lady Willingdon Hospital, Lahore have reported 30.5% incidence of endometrial carcinoma in patients presenting with postmenopausal bleeding[27]. The commonest type of endometrial carcinoma seen in our study was endometroid type (80%) which is close to that seen by Fatima *et al* in their study (81.8%)[17] but contrary was seen in a study done in 2018 at Ankara, Turkey where only 10% women were found to have endometroid type of carcinomas[28].

Considering the limitations in our study like small sample size, hospital based survey and lack of follow up by some patients, the results, however, cannot be generalized for the whole population.

CONCLUSION

Postmenopausal bleeding is an alarming symptom and should be thoroughly investigated with transvaginal ultrasound followed by endometrial biopsy for timely diagnosis and treatment.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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